CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022501Orig1s000

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:	October 8, 2010
Application Type/Number:	NDA 022501
To:	Scott Monroe, M.D., Director Division of Reproductive and Urologic Products
Through:	Zachary Oleszczuk, Pharm.D., Team Leader Denise Toyer, Pharm.D., Deputy Director Division of Medication Error Prevention and Analysis
From:	Tara Turner, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name, Label and Labeling Review
Drug Name(s):	Lo Loestrin Fe (Norethindrone Acetate and Ethinyl Estradiol Tablets, 1 mg/10 mcg Ethinyl Estradiol Tablets, 10 mcg and Ferrous Fumarate Tablets, 75 mg)
Applicant:	Warner Chilcott
OSE RCM #:	2010-1184 and 2009-652

CONTENTS

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Lo Loestrin Fe, is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Lo Loestrin Fe, acceptable in OSE Review #2009-2349, dated January 19, 2010. DDMAC reviewed the proposed name on December 17, 2009, and had no concerns regarding the proposed name from a promotional perspective. Furthermore, the Review Division did not have any concerns with the proposed name, Lo Loestrin Fe, during our initial review.

The Applicant received a complete response action for this NDA on January 26, 2010. The Applicant submitted a class 2 response on April 21, 2010. As part of that response, the Applicant submitted revised container labels, carton and insert labeling, which are also the subject of the current review. During the initial review cycle of this NDA, DMEPA completed a review of the Applicant's proposed labels and labeling in OSE Review #2009-652, dated January 14, 2010.

2 METHODS AND RESULTS

2.1 PROPRIETARY NAME

For the proposed proprietary name, DMEPA staff search 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 used in OSE Review #2009-2349 for the proposed proprietary name, Lo Loestrin Fe. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern.

Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN update. 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. As in the previous proprietary name review, DMEPA staff identified a United States Adopted Names (USAN) stem in the proposed proprietary name, as of October 4, 2010. The stem is -estr-, which represents estrogens.

The searches of the databases yielded no new names thought to look or sound similar to Lo Loestrin Fe and represent a potential source of drug name confusion.

2.2 LABELS AND LABELING

The Applicant submitted revised container labels (see Appendix A), carton (see Appendix B), and insert labeling on April 21, 2010. DMEPA used Failure Mode and Effects Analysis (FMEA) and the principles of Human Factors in our evaluation of the labels and labeling. We also reviewed the labeling recommendations presented in OSE Review #2009-652, dated January 14, 2010 to determine if our recommendations had been incorporated into the revised labels and labeling.

3 DISCUSSION

3.1 PROPRIETARY NAME

As noted in the previous proprietary name review of Lo Loestrin Fe, the root name, Loestrin, contains the USAN stem -estr-, which represents estrogens. Inclusion of a USAN stem in a proprietary name is typically unacceptable. However, in this case since the root name was approved in 1973, the presence of the USAN stem alone would not render the name unacceptable.

3.2 LABELS AND LABELING

The Applicant revised the labels and labeling and incorporated most of DMEPA's recommendations. However, changes in the presentation of the proprietary name and the product strength pose additional concerns.

4 CONCLUSIONS AND RECOMMENDATIONS

4.1 PROPRIETARY NAME

This re-review determined that the proposed name, Lo Loestrin Fe, is not vulnerable to name confusion that could 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, Lo Loestrin Fe, for this product at this time.

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 Reproductive and Urologic Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4.2 LABELS AND LABELING

Our evaluation noted areas where the presentation of information on the container labels, carton and insert labeling can be improved to minimize the potential for medication errors. We provide recommendations for all product labels and labeling in *Section 4.2.1 Comments to the Division* for discussion during the review team's label and labeling meetings. *Section 4.2.2 Comments to the Applicant* contains our recommendations for the container labels and carton labeling. We request the recommendations in Section 4.2.2 be communicated to the Applicant prior to approval.

Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review. If you have further questions or need clarifications on this review, please contact Maria Wasilik, Project Manager, at 301-796-0567.

4.2.1 Comments to the Division

A. General Comments for All Labels and Labeling

1. As stated in our previous review, we defer to the clinical review team for a decision regarding inclusion of the statement "Lo Loestrin Fe provides 26 days of active therapy" since it is unclear whether the 2 tablets containing ethinyl estradiol alone provide oral contraceptive efficacy. If the statement is included, it should be presented with less prominence than the proprietary name, established name, and product strength.
2. Consider revising the font used to present the proprietary name. As currently presented, the font is fanciful and may be difficult to read, especially the capital letter 'F', which may be confused as a capital letter 'T'.

4.2.2 Comments to the Applicant

A. Container Labels: Blister Card: Trade and Sample (28 tablets)

1. Remove the (b) (4) separating the proprietary name from the established name as this line is considered intervening matter and violates 21 CFR 201.10(a).
2. Increase the prominence of the proprietary name. As currently presented, it has less prominence than the manufacturer's logo.

3. Present the product strength on the blister card. As currently presented, the strength is missing.

B. Carton Labeling: Trade (5 blister cards per carton); Sample (1 blister card per carton; 6 cartons per tray)

1. Remove the [redacted](b) (4)" separating the proprietary name from the established name as this line is considered intervening matter and violates 21 CFR 201.10(a).
2. On the trade carton, relocate the statement "Ferrous fumarate tablets are not USP for dissolution and assay" (located in the upper left-hand corner of the principal display panel) to the back panel. As currently presented, this information is extraneous.
3. Present the product strength immediately after the established name on the principal display panel. As currently presented, the strength is only located on a side panel.

REFERENCES

1. ***OSE Review #2009-2349 Lo Loestrin Fe Proprietary Name Review, January 19, 2010, Turner, Tara.***

2. ***OSE Review #2009-652, Lo Loestrin Fe Label and Labeling Review, January 14, 2010, Turner, Tara.***

3. ***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.

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

USAN Stems List contains all the recognized USAN stems.

5. ***Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request***

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

5 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/ TS) immediately following this page

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

/s/

TARA P TURNER
10/08/2010

ZACHARY A OLESZCZUK
10/08/2010

DENISE P TOYER
10/08/2010

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:	January 19, 2010
To:	Scott Monroe, M.D., Director Division of Reproductive and Urologic Products
Through:	Zachary Oleszczuk, Pharm.D., Acting Team Leader Kellie Taylor, Pharm.D., MPH, Associate Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Tara Turner, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Lo Loestrin Fe (Norethindrone Acetate 1 mg and Ethinyl Estradiol 10 mcg tablets, Ethinyl Estradiol 10 mcg tablets, and Ferrous Fumarate 75 mg Tablets)
Application Type/Number:	NDA # 022501
Applicant:	Warner Chilcott
OSE RCM #:	2009-2349

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

CONTENTS

EXECUTIVE SUMMARY

Lo Loestrin Fe is the proposed proprietary name for norethindrone acetate and ethinyl estradiol tablets, ethinyl estradiol tablets, and ferrous fumarate tablets. This product represents an extension of the current Loestrin product line. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Lo Loestrin Fe, acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before approval of the NDA.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Warner Chilcott dated November 30, 2009 for an assessment of the proposed proprietary name, Lo Loestrin Fe, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The Applicant also submitted draft container labels, carton and insert labeling, which will be evaluated in a separate DMEPA review (see OSE RCM# 2009-652).

1.2 REGULATORY HISTORY

On April 9, 2009, the Applicant submitted (b) (4) as the proposed proprietary name for this product. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed name unacceptable because it does not provide adequate distinction from other combination products in the Loestrin product line. Subsequently, on September 21, 2009, the Applicant submitted (b) (4) (b) (4) which was determined by DMEPA to contain ambiguous modifiers. This information was communicated to the Applicant via teleconference on November 2, 2009 and the name was withdrawn. On November 11, 2009, the Applicant submitted (b) (4) which was determined by DMEPA to contain the USAN stem –estr-. This information was communicated to the Applicant via telephone call and the name was withdrawn. On November 30, 2009, the proposed proprietary name "Lo Loestrin Fe" was submitted and is the subject of the current review.

1.3 PRODUCT INFORMATION

Lo Loestrin Fe is indicated for the prevention of pregnancy in women (b) (4) (b) (4) The dosage of Lo Loestrin Fe is one blue tablet containing norethindrone acetate 1 mg and ethinyl estradiol 10 mcg daily for 24 consecutive days, followed by one white tablet containing ethinyl estradiol 10 mcg daily for 2 consecutive days, followed by one brown non-hormonal (placebo) tablet containing ferrous fumarate 75 mg daily for 2 consecutive days. The ferrous fumarate tablets do not serve any therapeutic purpose. All the tablets should be taken exactly as directed and at intervals not exceeding 24 hours. A patient should begin to take this product (b) (4) on the first day of her menstrual period (Day 1 Start) (b) (4) (b) (4) The product is supplied in cartons containing 5 blister cards (dispensers) of a 28-day regimen.

1.4 APPLICANT'S RATIONALE FOR PROPOSED NAME

In their proprietary name submission, the Applicant cites the following rationale for use of the proposed modifiers:

> *The modifier 'Lo' denotes the low amount of estrogen in this product when compared with other approved Loestrin products; the name Lo Loestrin Fe would accurately represent the fact that the new product provides the lowest estrogen regimen of all Loestrin products in the market. The modifier 'Fe' denotes the ferrous fumarate tablets (non-hormonal) provided to complete a 28-day cycle.*

2 METHODS AND MATERIALS

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

2.1 SEARCH CRITERIA

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.[1,2]

To identify drug names that may look similar to Lo Loestrin Fe, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. In this case, we evaluated the root name 'Loestrin' separately and in conjunction with the additional descriptor segments of the name ('Lo' and 'Fe'): 'Lo' denotes the low amount of estrogen in this product compared to other approved Loestrin products. 'Lo' is used for other marketed oral contraceptive products (and in some proposed names) to describe lower estrogen content, lower estrogen and progestin content, or lower dose in general (see Appendices D and E). For these uses, it is placed at the beginning, in the middle, or at the end of the proprietary name. 'Fe' is used to describe the non-hormonal component (i.e. ferrous fumarate) and is commonly used within the Loestrin product line (see Appendix F) and for other oral contraceptive products.

Specific attributes taken into consideration include the length of the name (twelve letters; three words), upstrokes (four: two capital letters 'L', capital letter 'F', and lower case 't'), downstrokes (none), cross-strokes (two: lower case 't' and capital letter 'F') and dotted letters (one, lower case 'i'). Additionally, several letters in Lo Loestrin Fe may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Lo Loestrin Fe.

When searching to identify potential names that may sound similar to Lo Loestrin Fe, the DMEPA staff searches for names with similar number of syllables (6), stresses (LO lo-ES- trin ef- e or LO lo-es-TRIN ef- e or LO LO-es-trin ef- e), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (see Appendix B). The Applicant's intended pronunciation (lō lō-ĕs'trĭn ĕf-ē) was also taken into consideration, as it was included in the

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

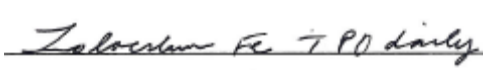
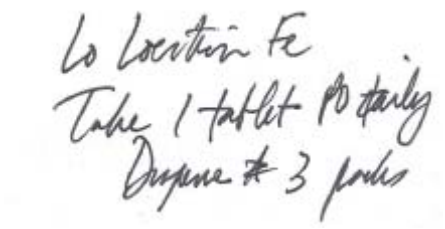
[2] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

Proprietary Name Review Request. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Lo Loestrin Fe Study (conducted on December 17, 2009)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	"Lo Loestrin Fe 1 tab PO daily"
Outpatient Prescription: 	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 26 names as having some similarity to the proposed proprietary name, Lo Loestrin Fe.

Ten of the names were thought to look like Lo Loestrin Fe (Halotestin, Colocort, Lo Ovral, Norlestrin 21 1/50, Norlestrin 21 2.5/50, Norlestrin 28 1/50, Norlestrin Fe 1/50, Norlestrin Fe 2.5/50, Lotensin, and Clobetasol). One name (Elestrin) was thought to sound like Lo Loestrin Fe. The remaining fifteen names (Loestrin 24, Loestrin 24 Fe, Loestrin, [redacted] (b) (4) Loestrin Fe 1.5/30, Loestrin Fe 1/20, Loestrin Fe, Loestrin 1.5/30, Loestrin 1/20, Loestrin 21 1/20, Loestrin 21 1.5/30, Loestrin 21, Lo Estrin Fe 24, and Lo Estrin Fe) were thought to look and sound similar to Lo Loestrin Fe.

Our searches also revealed that the proposed root name, Loestrin, is trademarked in the U.S. by Warner-Lambert Company and in several foreign countries by Parke Davis and Company, Galen Chemicals Ltd., or Warner Chilcott Company, Inc.

Additionally, DMEPA staff identified a United States Adopted Names (USAN) stem in the proposed proprietary name, as of December 17, 2009. The stem is –estr-, which represents estrogens.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Lo Loestrin Fe. The Expert Panel discussed the following concerns with the "Lo" modifier: "Lo" may be overlooked; what does "Lo" convey?; "Lo" can look like the number "10"; "Lo" may be interpreted as a stutter and omitted when transcribed from verbal orders; seems like a typographical error with double "Lo".

Additionally, the Expert Panel indicated that either of the modifiers ("Lo" or "Fe") could be omitted from prescriptions or medication orders.

Finally, the Expert Panel identified several definitions for the medical abbreviation "Lo": lateral oblique, linguo-occlusal, low lumber orthosis, lenticular opacity, leucine oxidation, and loss.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

For the study conducted on December 17, 2009, a total of 25 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Nine of the participants interpreted the drug name correctly as "Lo Loestrin Fe" or "Loloestrin Fe", with the majority of correct interpretations occurring in the outpatient written study and the verbal study. The remainder of participants misinterpreted the drug name. Approximately half of the misinterpretations in the inpatient written study involved the transcription of the first letter as "Z" instead of "L" followed by various misspellings. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF REPRODUCTIVE AND UROLOGIC PRODUCTS (DRUP)

3.4.1 Initial Phase of Review

In a response to the OSE December 17, 2009 e-mail, the Division of Reproductive and Urologic Products (DRUP) indicated that they had no comments regarding the proposed proprietary name, Lo Loestrin Fe.

3.4.2 Midpoint of Review

On December 23, 2009, DMEPA notified the Division of Reproductive and Urologic Products (DRUP) via e-mail that we had no objections to the proposed proprietary name Lo Loestrin Fe. Per e-mail correspondence from the Division of Reproductive and Urologic Products on December 23, 2009, they indicated that they concur with our assessment of the proposed proprietary name, Lo Loestrin Fe.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified one additional name which was thought to look similar to Lo Loestrin Fe and represent a potential source of drug name confusion. That name is Loniten.

Additionally, we note that two of the identified names ((b) (4) were proposed names for the product under review which were found unacceptable by DMEPA. Further, we note that eight of the identified names are variations of the approved Loestrin product line (Loestrin 24, Loestrin, Loestrin Fe, Loestrin 1.5/30, Loestrin 1/20, Loestrin 21, Lo Estrin Fe 24, and Lo Estrin Fe). We assume that these names were reported incorrectly during the search process. They are already accounted for in the evaluation of the Loestrin product line.

As such, a total of seventeen names were analyzed to determine if the drug names could be confused with Lo Loestrin Fe and if the drug name confusion would likely result in a medication error.

Five names represent Loestrin products that are currently marketed (see Appendix F). The Loestrin product line will be discussed in detail in Section 4.

Three names lacked convincing orthographic and/or phonetic similarity and were not evaluated further (see Appendix G).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name, Lo Loestrin Fe, could potentially be confused with any of the nine remaining names and lead to medication errors. This analysis determined that the name similarity between Lo Loestrin Fe and the identified names was unlikely to result in medication errors with any of the nine products identified for the reasons presented in Appendices H through J. This assessment is supported in part by the lack of medication errors with the approved Loestrin products and other drug products.

4 DISCUSSION

Neither DDMAC nor the Division of Reproductive and Urologic Products had concerns with the proposed name, Lo Loestrin Fe. DMEPA did not identify factors, other than names with potential similarity to Lo Loestrin Fe, that would render the name unacceptable.

4.1 USE OF "LO" AND "FE" MODIFIERS

As part of our FMEA we evaluated the potential for medication errors to occur due to misinterpretation of the modifiers "Lo" and "Fe".

4.1.1 Precedence

We note that the proposed name includes the modifiers "Lo" and "Fe", and that no data was provided to support that the modifiers would not inadvertently introduce a source of error. However, we also note that the "Fe" modifier is used consistently within the Loestrin product line, as well as for other approved oral contraceptives, to represent the ferrous fumarate component. In our review of the proposed name (b) (4) (see RCM #2009-651, dated July 8, 2009), DMEPA conducted a search of the FDA Adverse Event Reporting System (AERS) to identify potential problems with the nomenclature of the Loestrin product line. At that time we retrieved seven reports involving confusion between the strengths of the Loestrin Fe products, (b) (4) No cases of confusion between Loestrin Fe and the non-iron containing Loestrin products were identified, which helps to support the safety of the "Fe" modifier.

Similarly, the "Lo" modifier is used for other approved oral contraceptive products to represent lower estrogen content or lower estrogen and progestin content. The Applicant's intended meaning of the "Lo" modifier for the proposed product follows this established trend because we know how much estrogen Lo Loestrin Fe provides, which is lower on a daily and monthly basis than the other Loestrin products (see Appendix F).

Therefore, although this Applicant has not provided data to support the use of the proposed modifiers, DMEPA believes that the post-marketing experience with the Loestrin product line and the consistent use of the proposed modifiers with other approved products adequately supports their use for the proposed product. Thus, in consideration of the total data available, DMEPA does not object to the use of the modifiers, "Lo" and "Fe".

4.1.2 Other Safety Concerns

The CDER Expert Panel discussed the following concerns with the "Lo" modifier: "Lo" may be overlooked; what does "Lo" convey?; "Lo" can look like the number "10"; "Lo" may be interpreted as a stutter and omitted when transcribed from verbal orders; seems like a typographical error with double "Lo".

Additionally, the Expert Panel indicated that either of the modifiers ("Lo" or "Fe") could be omitted from prescriptions or medication orders. We note post-marketing evidence has shown that the omission of modifiers is a phenomenon that contributes to medication errors. However, post-marketing evidence has also shown that placement of the modifier as a prefix or infix, as opposed to a suffix, decreases the risk of such errors. Because there are five marketed Loestrin products, the omission of any of the modifiers on a prescription or medication order would require clarification from the prescribing healthcare practitioner before dispensing a product, thus preventing a dispensing error. Similarly, if the modifier 'Lo' was misinterpreted as the number '10' on a prescription or medication order, a pharmacist would need to seek clarification of the order since '10' is not a modifier utilized for the currently marketed Loestrin product line. This clarification would prevent a dispensing error.

Finally, the Expert Panel identified several definitions for the medical abbreviation "Lo": lateral oblique, linguo-occlusal, low lumber orthosis, lenticular opacity, leucine oxidation, and loss. However, these terms are not typically used in prescribing and dispensing medications.

4.2 ANALYSIS OF ROOT NAME "LOESTRIN"

Nine names were evaluated for their potential similarity to the proposed root name, Loestrin. The FMEA indicates that the proposed root name is not likely to result in name confusion that could lead to medication errors. This assessment is supported in part by the lack of medication errors with the approved Loestrin products and other drug products.

We note that the root name, Loestrin, contains the USAN stem –estr-, which represents estrogens. Inclusion of a USAN stem in a proprietary name is typically unacceptable. However, in this case since the root name was approved in 1973, the presence of the USAN stem alone would not render the name unacceptable.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Lo Loestrin Fe, is not vulnerable to name confusion that could lead to medication errors, nor is it promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Lo Loestrin Fe, 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, 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. If the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

If you have further questions or need clarifications, please contact Maria Wasilik, Regulatory Project Manager, at 301-796-0567.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Lo Loestrin Fe, and have concluded that it is acceptable.

Lo Loestrin Fe will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

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

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

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

3. Phonetic and Orthographic Computer Analysis (POCA)

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

4. 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.

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

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

6. 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.

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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and 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. U.S. Patent and Trademark Office (http://www.uspto.gov)

Provides information regarding patent and trademarks.

10. 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.

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

12. 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.

13. 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.

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.lexi.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:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [3]

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [4] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products

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[3] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

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

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

because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• 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	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a

variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary

name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?"***

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

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

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not

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

ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

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 PROPRIETARY 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 the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
5. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

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

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

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

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

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in root name, Loestrin	Scripted may appear as	Spoken may be interpreted as
Capital 'L'	Capital 'Z', 'F', 'T', 'C', or 'I'	
'o'	'e', 'a', 'u', or number '0'	'All' or any vowel
'e'	'i'	Any vowel
's'	'a' or 'n'	'x' or 'z'
't'	'l', 'b', or 'x'	'd'
'r'	'n', 'v', or 'x'	
'i'	'e'	Any vowel
'n'	'u', 'v', 'h', 's', 'r', or 'x'	'dn', 'gn', 'kn', 'mn', or 'pn'
Capital 'F'	Capital 'T', 'L, or 'Z'	's'

Appendix C: Lo Loestrin Fe Prescription Study Responses

Inpatient Medication Order	Voice Prescription	Outpatient Prescription
Loestrin Fe	Lo Loestrin FE	Lo Estrin Fe
Loloc--- Fe	Loestrin Fe	Lo loertrin Fe
Lolocslum FE	Loestrin FE (It sounded like Loloestrin, but I thought that was a mistake in the recording.)	Lo Loertrin Fe
Loloestrin Fe	Lo-Loestrin FE	Lo Loestrin FE
Lolostrin Fe	Lo-loestrin Fe	Lo Loestrin Fe
Zodocilum		Lo Loestrin Fe
Zoloatim Fe		Lo Loestrin Fe
Zolocslaw FE		Lo Loestrin Fe
Zoloeslam Fe		
Zoloeslan		
Zoloestim FE		
Zoloestrin Fe		

Appendix D: Marketed products with 'Lo' or 'Low' modifier in the name

Proprietary Name	Established Name	Modifier meaning	Regulatory Status
Ortho Tri-Cyclen Lo	Ethinyl estradiol and Norgestimate	Lower estrogen content than Ortho Tri-Cyclen	Approved 8/22/02; DMEPA objected to name
Tri-Lo-Sprintec	Ethinyl estradiol and Norgestimate	Lower estrogen content than Tri-Sprintec	Approved 6/29/09; DMEPA found name acceptable
Low-Ogestrel-21 Low-Ogestrel-28	Ethinyl estradiol and Norgestrel	Lower estrogen and progestin content than Ogestrel	Approved 7/28/99; DMEPA did not review names
Lo/Ovral Lo/Ovral-28	Ethinyl estradiol and Norgestrel	Lower estrogen and progestin content than Ovral	Approved 3/17/75 & 3/16/76; DMEPA did not review names
LoSeasonique	Ethinyl estradiol and Levonorgestrel	Lower estrogen and progestin content than Seasonique	Approved 10/24/08; DMEPA found name acceptable

Appendix E: Names with 'Lo' or 'Low' modifier that have never been marketed in the U.S.

Proprietary Name	Established Name	Modifier meaning	Regulatory Status
(b) (4)	Ethinyl estradiol and Levonorgestrel	Lower content of estrogen and progestin than Seasonale	DMEPA objected to name; NDA (b) (4) withdrawn effective 4/6/06
Lo Seasonale***	Ethinyl estradiol and Levonorgestrel	Lower content of estrogen and progestin than Seasonale	DMEPA found name acceptable; NDA (b) (4) withdrawn effective 4/6/06
(b) (4)	Ethinyl estradiol and Norgestimate	Lower estrogen content than Tri-Sprintec	DMEPA objected to name; ANDA 76-784 approved 6/29/09 as Tri Lo Sprintec
Femhrt Lo*** (hormone replacement therapy)	Ethinyl estradiol and Norethindrone acetate	Lower content of estrogen and progestin	DMEPA objected to name; NDA 21-065 approved 10/15/99; both strengths managed as Femhrt
(b) (4) (contraception; treatment of endometriosis)	Medroxyprogesterone acetate injectable suspension	Lower dose than Depo-Provera	DMEPA objected to both names; NDA 21-583 and 21-584 approved 12/17/04 and 3/25/05 as Depo-subQ Provera 104

Appendix F: Loestrin product line comparison

Product Name	Lo Loestrin Fe***	Loestrin 24 Fe	Loestrin Fe 1/20	Loestrin Fe 1.5/30	Loestrin 21 1/20	Loestrin 21 1.5/30
Combination tablets **Norethindrone acetate (NA) and Ethinyl estradiol (EE)**	**NA 1 mg/ EE 10 mcg** **(24 tablets)**	NA 1 mg/ EE 20 mcg (24 tablets)	NA 1 mg/ EE 20 mcg (21 tablets)	NA 1.5 mg/ EE 30 mcg (21 tablets)	NA 1 mg/ EE 20 mcg (21 tablets)	NA 1.5 mg/ EE 30 mcg (21 tablets)
Ethinyl estradiol (EE) tablets	**EE 10 mcg** **(2 tablets)**					
Ferrous fumarate tablets	**FF 75 mg** **(2 tablets)**	FF 75 mg (4 tablets)	FF 75 mg (7 tablets)	FF 75 mg (7 tablets)		
Monthly estrogen content	**260 mcg EE**	480 mcg EE	420 mcg EE	630 mcg EE	420 mcg EE	630 mcg EE

Appendix G: Names lacking convincing look-alike or sound-alike similarities with Lo Loestrin Fe

Proprietary Name	Source
Colocort	EPD
Lo Ovral	EPD
Clobetasol	EPD

Appendix H: Products not currently marketed in the U.S. (no generics available)

Proprietary Name	Similarity to Lo Loestrin Fe	Description	Application Status (per DARRTS)
Norlestrin 21 1/50	Orthographic	Ethinyl estradiol 0.05 mg and Norethindrone acetate 1 mg tablets NDA 016749	AIP
Norlestrin 21 2.5/50	Orthographic	Ethinyl estradiol 0.05 mg and Norethindrone acetate 2.5 mg tablets NDA 016852	AIP
Norlestrin 28 1/50	Orthographic	Ethinyl estradiol 0.05 mg and Norethindrone acetate 1 mg tablets NDA 016723	AIP
Norlestrin Fe 1/50	Orthographic	Ethinyl estradiol 0.05 mg and Norethindrone acetate 1 mg tablets; Ferrous fumarate 75 mg tablets NDA 016766	AIP
Norlestrin Fe 2.5/50	Orthographic	Ethinyl estradiol 0.05 mg and Norethindrone acetate 2.5 mg tablets; Ferrous fumarate 75 mg tablets NDA 016854	AIP

Appendix I: Products with no overlap in strength or dose

Lo Loestrin Fe		**Tablets: (norethindrone acetate and ethinyl estradiol tablets 1 mg/10 mcg, ethinyl estradiol tablets 10 mcg, and ferrous fumarate tablets 75 mg)**	**One tablet orally once daily**
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Lotensin product line	Orthographic	Lotensin (benazepril hydrochloride) tablets: 5 mg, 10 mg, 20 mg, 40 mg Lotensin HCT (benazepril and hydrochlorothiazide) tablets: 5 mg/6.25 mg; 10 mg/12.5 mg; 20 mg/12.5 mg; 20 mg/25 mg	Lotensin: Initially, 10 mg orally once daily. The usual dosage is 20 to 40 mg per day given in one to two divided doses. Maximum dosage is 80 mg per day. Lotensin HCT: A patient whose blood pressure is not adequately controlled with either benazepril or hydrochlorothiazide alone may be given the combination product, usually one tablet of 10 mg/12.5 mg or 20 mg/12.5 mg orally once daily. Titrate based on clinical response, up to two tablets of 20 mg/25 mg per day.
Loniten (*Brand name product discontinued; generics available)	Orthographic	Minoxidil tablets: 2.5 mg, 10 mg	Inittially, 5 mg orally given as a single daily dose. The dosage may be increased in intervals of at least 3 days to 10 mg, 20 mg, and then to 40 mg in single or divided doses for optimum blood pressure control. The usual effective dose range is 10 to 40 mg per day, given in one to two divided doses.

Appendix J: Products with overlap in dose and dosage form.

Failure Mode: Name confusion	Causes (could be multiple)	Effects
Lo Loestrin Fe	**Tablets: (norethindrone acetate and ethinyl estradiol tablets 1 mg/10 mcg, ethinyl estradiol tablets 10 mcg, and ferrous fumarate tablets 75 mg)**	**One tablet orally once daily**
Halotestin (fluoxymesterone) tablets 2 mg, 5 mg, 10 mg *Brand name product discontinued; only the 10 mg strength is currently available as a generic	Orthographic similarity ('estin' vs. 'estrin'; 'halo' vs. 'lolo') Overlapping frequency (once daily) Overlapping dosage form and route of administration (oral tablets) Single strength	The orthographic differences in the names help to minimize the risk of medication errors in the usual practice setting. Although the names contain ending letters which may look similar when scripted ('estin' vs. 'estrin'), the beginning letters do not look alike, especially when written in upper case ('Halo' vs. 'LoLo'). Additionally, the modifier 'Fe' helps to differentiate the names. The risk of medication errors is further reduced by the different dosage regimens. The recommended dose of Halotestin ranges from 2.5 mg to 20 mg per day, depending upon the condition being treated. The total daily dose may be given in divided doses, one to four times daily. Given that the brand product is no longer commercially available, and the generic product is only available in the 10 mg strength, tablets may need to be divided or given in multiples to meet the dosage recommendations. By contrast, Lo Loestrin Fe is dosed one tablet orally once daily.
Elestrin (estradiol) Gel 0.06%	Phonetic similarity ('loestrin' vs. 'elestrin') Overlapping frequency (once daily) Overlapping directions (patients may be instructed to use or take once daily as directed) Single strength	The phonetic differences in the names help to minimize the risk of medication errors in the usual practice setting. Although the names contain letters which may sound similar when spoken ('loestrin' vs. 'elestrin'), the modifiers 'Lo' and 'Fe' help to differentiate the names. The risk of medication errors is further reduced by the differing product characteristics. Elestrin is a topical gel which is applied to the upper arm. The initial dose is one pump daily. Subsequent dosage adjustment (to two pumps daily) may be made based upon individual response. By contrast, Lo Loestrin Fe is a pack containing oral tablets and is dosed one tablet orally once daily.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22501	ORIG-1	WARNER CHILCOTT CO INC	(b) (4)

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