CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-048/22-223

PROPRIETARY NAME REVIEW(S)

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
HFD-420; WO 22; Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL AND LABELING REVIEW

DATE OF REVIEW: November 27, 2007

NDA #: 22-048 (IND# [redacted]

NAME OF DRUG: **Triesence**
(Triamcinolone Acetonide) Injection
40 mg/mL

IND HOLDER: Alcon Research, Ltd.

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

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anti-Infective and Ophthalmology Products (HFD-520), for assessment of the proprietary name, Triesence, regarding potential name confusion with other proprietary or established drug names. Container labels, carton labeling were submitted for review and comment at this time.

PRODUCT INFORMATION

Triesence is a 505(b)(2) application that provides for a terminally sterilized and unpreserved ophthalmic triamcinolone acetonide. The reference listed drugs are Kenalog-40 (NDA 14-901) and Nasacort HFA (NDA 20-784).

Triesence is a synthetic corticosteroid indicated for the treatment of [redacted] sympathetic ophthalmia, temporal arteritis, uveitis, ocular inflammatory conditions unresponsive to topical corticosteroids [redacted]. Triesence is also indicated for visualization during vitrectomy. The initial recommended dose for the treatment of ophthalmic conditions is 4 mg (0.1 mL) administered intravitreally, with subsequent doses of 4 mg (0.1 mL) as needed. For visualization during vitrectomy, the recommended dose is 1 mg to — mg intravitreally. Triesence will be supplied as a 1 mL vial.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of the internet, several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Triesence to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The Saegis[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches.

In addition, DMETS conducted three requisition analysis studies consisting of two handwritten requisition studies and one verbal requisition study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name. Following completion of these initial components, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics must be considered in the overall safety evaluator risk assessment.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Triesence. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name, Triesence, acceptable from a promotional perspective.

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[1] MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, and the electronic online version of the FDA Orange Book.
[4] Phonetic and Orthographic Computer Analysis (POCA)
[5] WWW location http://www.uspto.gov/tmdb/index.html.
[6] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

2. The Expert Panel identified eleven proprietary names that were thought to have the potential for confusion with Triesence. They are Triacin C, Trisenox, TriNessa, Tranxene, Triamterene, Trientine, Transacin, Tirazone, Trievacin, Triacet, and Ellence. An independent search identified one additional name, ——— ***. Additionally, one member of the Expert Panel noted that the name sounds like "Nutrients". Another member noted that Triesence is patented in Switzerland and the United Kingdom, and that Triesence is difficult to spell and would likely be misspelled.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Triesence with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten pharmacy requisition orders or verbal pronunciation of the drug name. These studies employed a total of 122 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Two pharmacy requisition orders were written, each consisting of a combination of marketed and unapproved drug products and an order for Triesence (see below). These orders were optically scanned and one order was delivered to a random sample of the participating health professionals via e-mail. In addition, one of the requisition orders was recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal requisition orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN REQUISITION	VERBAL REQUISITION
Requisition Sample A: Triesence 8 vials	Triesence 8 vials
Requisition Sample B: Triesence 8 vials	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See appendix A (page 10) for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Triesence, the following twelve names were identified as having similar sound and/or appearance to Triesence, Tri-Nessa, Trientine, Triamterene, Transacin, Triacet, Triacin C, Tranxene, Tirazone, Ellence, Trievacin, Trisenox and ——— ***.

Although a member of the Expert Panel noted Triesence sounded like "Nutrients", none of the verbal responses were misinterpreted as "Nutrients". Additionally, we can not foresee a clinical situation where the two names would be confused.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with either of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of interpretations were misspelled/phonetic variations of the proposed name, Triesence.

Upon review of the twelve names identified as potential look-alike and/or sound-alike names to Triesence, we determined the following nine names: Trientine, Triamterene, Transacin, Tranxene, Tirazone, Ellence, Triacet, Trievacin and Triacin-C would not be considered further for the following reasons.

- In addition to lacking orthographic and/or phonetic similarities with Triesence, Trientine, Triamterene, Transacin, Tranxene, Tirazone, Ellence, and Triacet do not share product commonalities such as dosage form, route of administration, product strength, usual dose, indication of use, context of use and/or prescription only status.
- The product Trievacin is an oral triphasic contraceptive marketed in Uruguay. Although Trievacin may look similar to Triesence, DMETS believes that the actual possibility for confusion between these product names to be minimal due to the areas of marketing.
- Triacin C was not reviewed further due to discontinuation of the product along with the fact that there are no generic equivalents available.

The remaining three names warranted further evaluation based upon their similar appearance as well as product characteristics (see Table 1 on page 6).

Table 1: Potential Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s); Established name	Usual adult dose	Other	Differing Product Characteristics
Triesence	Triamcinolone Acetonide Suspension for Intravitreal Injection 40 mg/mL	• 4 mg intravitreally with subsequent doses of 4 mg as needed over the course of treatment	NA	
Trisenox	Arsenic Trioxide 1 mg/mL Injection	• Initial: 0.15 mg/kg; Intravenously daily over 1-2 hours.	LA	No overlap • **Product Strength** ➢ 40 mg/mL vs. 1 mg/mL • **Dosing** ➢ Patient specific dosage-based upon patient weight (0.15 mg/kg) vs. 4 mg • **Route of Administration** ➢ Intravitreally vs. Intravenous • **Indication of Use** ➢ Treatment of ophthalmic conditions vs. Acute promyelocitic leukemia
TriNessa	Ethinyl Estradiol 35 mcg and Norgestimate 0.18 mg, 0.215 mg, or 0.25 mg	1 tablet daily	LA	No overlap • **Product Strength** ➢ 40 mg/mL vs. 0.035 mg/0.18 mg, 0.215 mg or 0.25 mg • **Usual Dosage** ➢ 4 mg vs. 1 tablet • **Route of Administration** ➢ Intravitreally vs. Oral • **Dosage Form** ➢ Injectable vs. Tablet • **Indication of Use** ➢ Treatment of ophthalmic conditions vs. oral contraception
[redacted]	[redacted]	[redacted]	LA	• **Discussed below.**

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)

Upon further analysis of the three names, Trisenox, TriNessa and [redacted]***, the names Trisenox and TriNessa were considered to have minimal risk of confusion while [redacted]*** needed further evaluation. The reasons Trisenox and TriNessa were not considered further are described in the Differing Product Characteristics column of Table 1 above. [redacted] *** is discussed in detail below.

III. LABELING, PACKAGING AND SAFETY RELATED ISSUES:

In the review of the insert labeling for Triesence, DMETS conducted a failure mode and effects analysis (FMEA) and applied principals of human factors. Our analysis has identified the following areas of improvement.

A. GENERAL COMMENTS

1. Presenting the proprietary name bolded and in a different font than the established name gives less prominence to the active ingredient information. Taking into account typography, layout, contrast, and other printing features (e.g., font size and type), revise the established name in accordance with CFR 201.10(g)(2) so that it has a prominence commensurate with the prominence of the proprietary name.

2. Since this is a single use vial, revise to include the statement "Discard any unused portion" to minimize the risk of reuse of the vial.

3. To minimize the risk of administration by an improper route, revise to include the route of administration statement "For Intravitreal Use Only".

4. Increase the size of the product strength to improve the readability of this important information.

5. Currently the strength is not presented on the front display panel in a prominent manner. Typically this information appears following the established name because it allows for increased recognition. Please revise so that the trade name, established name, and product strength are presented in the following manner throughout the labels and labeling:

   Triesence
   (Triamcinolone Acetonide Injection)
   40 mg/mL

B. CONTAINER LABEL

1. See General Comments A1 through A5. To allow for these revisions to the container label, the "Rx only", storage and "sterile" statements may be deleted per 21 CFR 201.10(i).

2. Decrease the prominence and debold the manufacturer's name as it is more prominent than important statements such as the proprietary name, established name and product strength.

C. BLISTER LABELING

See General Comments A2 through A5.

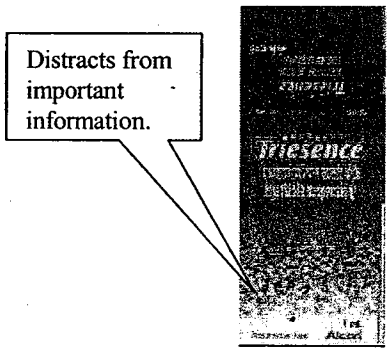
D. CARTON LABELING

1. See General Comments A1 through A5.

2. Delete the graphic (i.e., the trailing off of the letter "i") that appears above the proprietary name as this may be a visual distraction away from important information such as the proprietary name, established name and product strength.

3. Relocate the "RX only statement to the principal display panel.

4. When the carton is revised to include the strength immediately following the proprietary and established names (see A5 above), the use of the two colors (i.e., blue and white) should not obscure or distract from the presentation of the strength. Revise accordingly.



E. INSERT LABELING

The volume of Triesence to be administered should be expressed in a unit of measure that practitioners are familiar with, understand, and can easily measure with a commonly stocked syringe. Thus, revise volumes expressed in "µL" in the Dosage and Administration sections so they are expressed in "mL" (e.g., "100 µL" should be revised to read "0.1 mL"). Additionally, the abbreviation "µL" has been misinterpreted as "mL" (the abbreviation for milliliter).

Appendix A

Inpatient	Outpatient	Voice
Fressence	Triescence	Triacin
Friesence	Triesence	Triacin
Friesence	Triesence	Triasin
Tresence	Triesence	Triasin
Triasence	triesence	Triasyn
Triesence	Triesence	Triesence
Triesence	Triesence	Triessen
Triesence	Triesence	Triessen
Triesence	Triesence	Triessence
Triesence	Triesence	Triessence
Triesence	Triesence	
Triesence	Triesence	
Triesence	Triesence	
Triesence	Triesenee	
Triesence	Triesenu	
Triesence	Trisence	
Triesence		
Trusence		

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/s/

Diane Smith
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CSO

Todd Bridges
11/27/2007 04:10:45 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
11/27/2007 04:43:51 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
11/27/2007 04:45:15 PM
DRUG SAFETY OFFICE REVIEWER