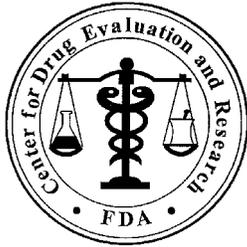


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-437

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: July 22, 2009

To: Robert Justice, MD, Director
Division of Drug Oncology Product

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

From: Cathy A. Miller, BSN, MPH, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Reconsideration Review

Drug Name(s): Trelstar (Triptorelin Pamoate) For Injectable Suspension
3.75 mg, 11.25 mg and 22.5 mg

Application Type/Number: NDA 22-437
NDA 20-715/S-018
NDA 21-288/S-015

Applicant: Watson Laboratories, Inc.

OSE RCM #: 2009-893, 2009-920 and 2009-921

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In This Document**

CONTENTS

1. INTRODUCTION.....	3
1.1. Regulatory History.....	3
2. MATERIAL REVIEWED.....	4
3. RESULTS AND DISCUSSION.....	3
3.1. Labels and Labeling.....	3
3.2. Revised Communication and Marketing Plan.....	3
4. CONCLUSIONS AND RECOMMENDATIONS	4
4.1. Comments to the Division.....	4
4.2. Comments to the Applicant.....	5
5. REFERENCES	5

1 INTRODUCTION

The Division of Medication Error Prevention and Analysis (DMEPA) reviewed the Applicant's amendment to the pending application NDA 22-437 for the reconsideration of the proposed proprietary name, Trelstar, submitted on May 4, 2009, along with prior approval supplement name change proposals for NDA 20-715/S-018 and 21-288/S-015. These submissions reflect recommendations discussed during the April 22, 2009 teleconference between the Applicant, the Division of Drug Oncology Products (DDOP) and DMEPA regarding the Agency's concerns with managing the three applications under the proprietary name 'Trelstar'.

1.1 REGULATORY HISTORY

On October 20, 2008, the Applicant submitted A new drug application (NDA 22-437) for a third product strength (22.5 mg) requesting the review of proposed proprietary name 'Trelstar' (b)(4). This product is dosed every 24 weeks, and differs in formulation from the 3.75 mg and 11.25 mg strengths. After their review of this proposed proprietary name, the Division of Drug Marketing, Advertising and Communication (DDMAC) objected to the name 'Trelstar' (b)(4), stating: (b)(4) of the drug product. Adding (b)(4) to "Trelstar" (b)(4) for its approved indication, the palliative treatment of advanced prostate cancer. The DDMAC objection was communicated to the Applicant on November 12, 2008. Subsequently, the Applicant amended their application on December 22, 2008, requesting the review of proposed proprietary name 'Trelstar' for the new drug application 22.5 mg strength.

On December 29, 2008, the Applicant also submitted prior approval supplements to the currently marketed Trelstar Depot (3.75 mg strength, NDA 20-715/S-018) and Trelstar LA (11.25 mg strength, NDA 21-288/S-015), requesting the deletion of the suffixes 'Depot' and 'LA', thus proposing that the product line of all three strengths (3.75 mg, 11.25 mg and 22.5 mg) fall under the single proposed proprietary trade name 'Trelstar'.

DMEPA completed our proprietary name review of these submissions and found the proposal to manage all three strengths under the name 'Trelstar' unacceptable. DMEPA objected to the name 'Trelstar' due to concerns that product confusion and inappropriate substitution may occur between the 22.5 mg strength and the currently marketed 3.75 mg and 11.25 mg strength products. Both DMEPA and DDOP had concerns that by using the name 'Trelstar' alone for all three product strengths, clinicians may mistakenly conclude that the three products vary only in their strength and can be used interchangeably, and combine smaller strengths to an achievable 22.5 mg dose (i.e. 2 X 11.25 mg). On March 23, 2009, DDOP issued a letter to the Applicant communicating our objection to the proposed proprietary name, Trelstar, for the pending 22.5 mg strength. On March 31, 2009, DDOP issued a letter for the prior approval supplement name changes for Trelstar LA and Trelstar Depot which objected to the name change.

On April 2, 2009, the Applicant submitted a general correspondence to DDOP requesting a reconsideration of the FDA position and recommendation regarding the proprietary name citing precedence for similar nomenclature plans for other products with extended-

release formulations available in more than one strength (i.e. Eligard and Zoladex) and managed under a single proprietary name. The Applicant requested a teleconference to further discuss their Trelstar nomenclature plan. On April 22, 2009, a teleconference was held between DMEPA, DDOP and Watson Pharmaceuticals. As a result of these discussions, DMEPA agreed with the rationale outlined by the Applicant conditional on the following submissions:

- 1) An integrated product insert label that reflects information on all three Triptorelin Pamoate strengths (3.75 mg, 11.25 mg and 22.5 mg).
- 2) Revised container labels and carton labeling, with the frequency of use indicated in WEEKS displayed prominently on the principal display panel in addition to the strength, similar to the features illustrated on the Eligard product line.
- 3) Revise their Nomenclature Implementation plan to provide detailed clarifications of their marketing and communication plans to targeted parties of interest (healthcare providers, pharmacists, patients, etc) for the name changes to the current Trelstar Depot and Trelstar LA products, in conjunction with the introduction into the market of the pending third strength product.

On May 4, 2009, the Applicant submitted an amendment to the pending application (NDA 22-437) and the prior approval supplement name change requests for NDA 20-715 and 21-288, requesting a reconsideration for the proposed proprietary name, Trelstar, for all three strengths.

2 MATERIAL REVIEWED

For this review, the Applicant submitted on May 4, 2009 the following as part of their request for reconsideration for the proposed proprietary name, Trelstar. (See Appendices A through D for images):

- Container Label for Trelstar 3.75 mg, 11.25 mg and 22.5 mg
- Carton Labeling for Trelstar 3.75 mg, 11.25 mg and 22.5 mg
- Carton Labeling for Trelstar 3.75 mg, 11.25 mg and 22.5 mg Mixject
- Revised Communication and Marketing Plan for Trelstar Proprietary Name Change and Sample Dear Doctor Letter
- Combined Package Insert Labeling (no image)

DMEPA's review of labels and labeling submitted for this review concentrates on the evaluation of the nomenclature plan to incorporate product characteristics into the presentation of the proprietary name, in an effort to provide product distinction for the three Trelstar strengths. A full label and labeling risk assessment will be performed in separate forthcoming OSE reviews.

3 RESULTS AND DISCUSSION

3.1 LABELS AND LABELING

3.1.1 Container Labels and Carton Labeling

The revised container labels and carton labeling include the proprietary name ‘Trelstar’ with the strength adjacent to the name, along with descriptors stating the strength and frequency (3.75 mg every 4 weeks, 11.25 mg every 12 weeks, and 22.5 mg every 24 weeks) clearly displayed in a colored boxes (varying for each strength) below the proprietary and established name.

The presentation of proprietary name, strength and frequency of administration provides emphasis to the product strength and frequency of use. DMEPA believes that this presentation provides product distinction and may help avert confusion related to product selection and administration. We believe these features will prompt health care providers who may be more familiar with the currently marketed products by the names ‘Trelstar Depot’ and ‘Trelstar LA’ since their strengths ‘3.75 mg and 11.25 mg’ and frequency of administration ‘every 4 weeks’ and ‘every 12 weeks’ are clearly displayed on product labels and labeling. The added features may also help avert the potential for combining lower strengths to an achievable higher strength (i.e. 2 X 11.25 mg to achieve a 22.5 mg strength).

3.1.2 Combined Package Insert Labeling

The Applicant’s revised package insert labeling combines insert labeling information for all three Trelstar strengths and is presented throughout package insert labeling with the name ‘Trelstar’, along with the strength and frequency of administration: 3.75 mg every 4 weeks, 11.25 mg every 12 weeks and 22.5 mg every 24 weeks. A label and labeling risk assessment of the revised package insert labeling will be evaluated in a separate OSE Review.

3.2 REVISED COMMUNICATION AND MARKETING PLAN

The Applicant’s revised plan outlines their proposal to implement a communication and marketing plan for all three Trelstar strengths within 90 days after approval of the new drug application for NDA 22-437. The Applicant stipulates that their plan assumes the approval of the pending NDA and the proprietary name changes for the 3.75 mg and 11.25 mg strengths will occur on or before the 22.5 mg strength application PDUFA date of July 12, 2009. They state that the plan further assumes that the launch of the new Trelstar 22.5 mg strength and the announcement of the name changes will occur on or before October 2009 to ensure that Watson Pharmaceuticals has sufficient time to develop, approve and deliver these communications.

3.2.1 Communication Plan

The Applicant has identified a variety of InfoAlerts, correspondence, announcements, and other forms of communication designed to disperse information regarding the Trelstar line. They plan to contract with (b) (4) to create supplement mailings for all

Trelstar strengths, as well as drug information databases such as First Data Bank and Redbook. The Applicant's Marketing Plan includes visual aids, combined package inserts and instruction materials provided with the Mixject, along with additional marketing tactics to communicate the new Trelstar 22.5 mg strength, in conjunction with the 3.75 mg and 11.25 mg strength name changes, through journal advertisements, patient education pamphlets, hospital displays, product monographs and others.

As part of their plan, the Applicant has provided a sample 'Dear Doctor' letter designed to both, inform providers about the new 22.5 mg strength, as well as alert them about the name changes of the two currently marketed strengths (See Appendix E). The letter includes before and after picture images of the 3.75 mg and 11.25 mg container labels along with narrative information describing the name change, along with product strength and frequency of administration clarification, which may provide added product distinction to providers who are familiar with the currently marketed products, Trelstar Depot and Trelstar Depot.

3.2.2 Marketing Plan

Additionally, the Applicant proposes a transition from current product packaging to new product packaging including package insert labeling, product cartons, vial labels and outer packing cartons to comply with the approval of Trelstar 22.5 mg (24 Weeks) and the name change from Trelstar Depot and Trelstar LA to Trelstar, with the accompanying strength and frequency presented in labeling, Trelstar 3.75 mg (4 Weeks) and Trelstar 11.25 mg (12 Weeks). The Applicant plans to start production of new packaging and integrated package inserts within 90 days of the approval of the prior approval supplements for the Trelstar LA and Trelstar Depot name changes.

The Applicant requests that the Agency allow a time window of approximately 180 days to distribute the product in the current packaging with current package inserts to customers to ensure reasonable time to utilize existing levels of finished goods inventory and to start stocking sufficient levels of finished goods inventory with new branded packaging and package inserts. DMEPA finds this request reasonable.

4 CONCLUSIONS AND RECOMMENDATIONS

4.1 COMMENTS TO THE DIVISION

DMEPA is satisfied that the Applicant's submission of the reconsideration of the proposed proprietary name, Trelstar, adequately provides product distinction between the three strengths through features added to labels and labeling that emphasize the product strength and frequency of administration, in conjunction with the presentation of the proprietary name. DMEPA will conduct a full label and labeling risk assessment for the pending application as well as the prior approval supplements for revisions to Trelstar Depot and Trelstar LA, in separate OSE Labeling Reviews.

Since the Applicant has also submitted prior approval supplement revisions for the reconsideration of the proposed name changes for Trelstar Depot and Trelstar LA to 'Trelstar' (NDA 20-715/S-018 and 21-288/S-015), along with revisions to container labels and carton labeling, any decisions regarding approval of those supplements should be simultaneously coordinated with decisions made regarding the pending application

(NDA 22-437) in order to effectively facilitate the timelines outlined in the Applicant's Revised Communication and Marketing Plan.

We will provide comments regarding labels and labeling in a separate review. If you have any questions or need clarifications, please contact Sandra Griffith, OSE Project Manager, at 301-796-2445.

4.2 COMMENTS TO THE APPLICANT

We have reviewed your request for reconsideration of the proposed proprietary name, Trelstar, for the pending application (NDA 22-437) along with the prior approval supplement for Trelstar Depot and Trelstar LA (20-715/S-018 and 21-288/S-015). Based on the materials submitted to support this proposal submitted on May 4, 2009, we find the proposed proprietary name, Trelstar, acceptable for all three strengths. However, our decision is contingent upon approval of NDA 22-437 and prior approval labeling supplements for Trelstar Depot and Trelstar LA.

5 REFERENCES

1. Reviews

OSE Review #2008-2046 Proprietary Name Review for Trelstar (Triptorelin Pamoate for Injectable Suspension) 22.5 mg, Miller, C; March 19, 2009.

OSE Review #2009-422 and #2009-424 Prior Approval Supplement Name Change Review for Trelstar Depot and Trelstar LA Triptorelin Pamoate for Injectable Suspension) 3.75 mg and 11.25 mg, Miller, C; March 20, 2009.

7 page(s) of Draft Labeling have been Withheld in Full immediately following this page as B4 (CCI/TS)

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

/s/

CATHY A MILLER
07/28/2009

KELLIE A TAYLOR
07/28/2009

DENISE P TOYER
07/30/2009

CAROL A HOLQUIST
07/30/2009



**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 19, 2009

To: Robert Justice, M.D., Director
Division of Drug Oncology Products

Through: Kellie Taylor, Pharm.D., M.P.H., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Error Prevention and Analysis

From: Cathy A. Miller, M.P.H.,
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name(s): Trelstar (Triptorelin Pamoate) For Injectable Suspension
22.5 mg

Application
Type/Number: NDA 22-437

Applicant: Watson Pharmaceuticals

OSE RCM #: 2008-2046

*****Note: This review 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	4
2 METHODS AND MATERIALS	6
2.1 Proprietary Name Risk Assessment	6
3 RESULTS.....	12
3.1 Proprietary Name Risk Assessment	12
4 DISCUSSION	16
4.1 Applicant Trade Name Implementation Plan.....	16
5 CONCLUSIONS AND RECOMMENDATIONS	16
5.1 Comments To The Division.....	17
5.2 Comments To The Applicant.....	17
6 REFERENCES	18
APPENDICES	20

EXECUTIVE SUMMARY

The applicant has proposed a new 22.5 mg strength of Triptorelin Pamoate, which is an extended-release formulation with a mechanism of action that is different from the currently marketed 3.75 mg and 11.25 mg strengths. We note that the sponsor has also requested to change the proprietary names of the already marketed Trelstar products, Trelstar Depot (NDA 20-715) and Trelstar LA (NDA 21-288) to “Trelstar”. DMEPA anticipates inappropriate product substitution may occur between the 22.5 mg strength and the currently marketed 3.75 mg and 11.25 mg if the products are managed under a single name. The medication errors we anticipate include wrong dose and wrong product selection errors.

As such, DMEPA finds the proposed name, Trelstar, vulnerable to confusion that could lead to medication errors for this product and the currently marketed products. DMEPA will provide additional comments to the Division in a separate memorandum to state our objection to the proposed proprietary name changes submitted in the Applicant’s December 29, 2008 prior approval supplements (NDA 20-715, S-018) and (NDA 21-288, S-015).

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Applicant, Watson Pharmaceuticals, on December 22, 2008, new drug application (NDA 22-437) for the proprietary name review of the proposed name, Trelstar, for the potential to contribute to medication errors. The Applicant also submitted container labels and carton labeling for review, which will be reviewed separately in OSE Review #2009-18.

1.2 REGULATORY HISTORY

Trelstar Depot (Triptorelin Pamoate) For Injectable Suspension, 3.75 mg, new drug application (NDA 20-715) was originally approved on June 15, 2000 for the palliative treatment of advanced carcinoma of the prostate. This formulation is dosed every month. DMEPA reviewed the proposed name ‘Trelstar Depot’ in OSE Review #00-0041 dated April 3, 2000, and found the name acceptable. At the time, no other formulations were under review by DMEPA.

On August 20, 2000, the Applicant submitted new drug application (NDA 21-288) for a second product strength (11.25 mg) dosed every 3 months, along with the request for proposed proprietary name ‘Trelstar LA’. At the time, there were no other Trelstar formulations under review by the Agency and the Applicant did not indicate their intentions to further develop the Trelstar product line. DMEPA evaluated the proposed proprietary name ‘Trelstar LA’ in OSE Review #00-240 dated February 23, 2001, and found the name acceptable, citing concerns, however, about the potential name confusion between Trelstar Depot and Trelstar LA as well as future concerns of product confusion if additional product strengths are added to the Trelstar line. At that time, DMEPA concluded that limited product distribution with administration only under the

supervision of a health care professional, along with other recommendations provided may minimize name confusion medication errors. DMEPA recommendations included that the Applicant adequately advise the healthcare community about the introduction of the new strength, and labels and labeling recommendations included emphasizing the frequency of use (“Give once every month” versus “Give once every 84 days”) on container labels, carton labeling and in package insert labeling.

On October 20, 2008, the Applicant submitted new drug application (NDA 22-437) for a third product strength (22.5 mg) requesting the review of proposed proprietary name ‘Trelstar (b)(4)’. This product is dosed every 24 weeks, and differs in formulation from the 3.75 mg and 11.25 mg strengths. After their review of this proposed proprietary name, the Division of Drug Marketing, Advertising and Communication (DDMAC) objected to the name ‘Trelstar (b)(4)’, stating (b)(4) of the drug product. DDMAC acknowledges that "Trelstar Depot" and "Trelstar LA" are currently on the market. However, adding (b)(4) to “Trelstar” (b)(4) for its approved indication, the palliative treatment of advanced prostate cancer. In the absence of substantial evidence to support (b)(4)

Please note that the Federal Food Drug and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made, whether through a proposed trade name or otherwise; this includes suggestions that a drug is better, more effective, useful in a broader range of conditions or patients, safer, has fewer, or lower incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n); 21 CFR 202.1(e)(5)(i);(e)(6)(i)].”

The DDMAC objection was communicated to the Applicant on November 12, 2008 and subsequently, the Applicant amended their application on December 22, 2008, requesting the review of proposed proprietary name ‘Trelstar’ for the new drug application 22.5 mg strength. On December 29, 2008, in conjunction with this request, the Applicant also submitted prior approval supplements to the currently marketed Trelstar Depot (3.75 mg strength, NDA 20-715, S-018) and Trelstar LA (11.25 mg strength, NDA 21-288, S-015), requesting the deletion of the suffixes ‘Depot’ and ‘LA’, thus proposing that the product line of all three strengths (3.75 mg, 11.25 mg and 22.5 mg) fall under the single proposed proprietary trade name ‘Trelstar’. The Applicant also provided proposed revisions to container labels, carton labeling and package insert labeling reflecting the name change to ‘Trelstar’ which will be reviewed separately in OSE Review #2009-18.

1.3 PRODUCT INFORMATION

Trelstar (Triptorelin Pamoate) for Injectable Suspension is indicated for the palliative treatment of advanced prostate cancer (b)(4)

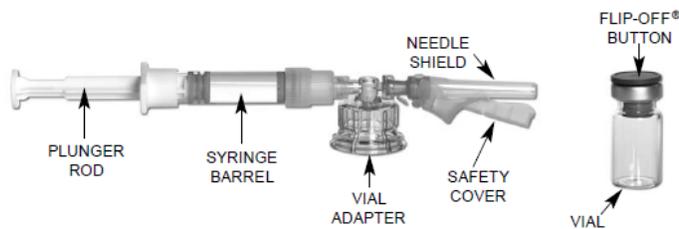
Triptorelin Pamoate is available in strengths for varying frequency of administration. The 3.75 mg strength (Trelstar Depot) is administered monthly, the 11.25 mg strength (Trelstar LA) is administered every 84 days, and the proposed 22.5 mg strength (proposed name Trelstar) is administered every 24 weeks. It is our understanding from DDOP that the Trelstar Depot and Trelstar LA are the same

formulations (but differ strengths, while the proposed “Trelstar”22.5 mg product differs in formulation and strength from the currently marketed Trelstar products.

Trelstar 22.5 mg will be supplied two ways, first in a single dose vial with a flip-off seal containing sterile lyophilized Triptorelin Pamoate microgranules, or in the Trelstar MIXJECT single-dose delivery system. The MIXJECT delivery system consists of a vial with a flip-off seal containing sterile lyophilized Triptorelin Pamoate microgranules, a MIXJECT vial adapter, and a pre-filled syringe containing sterile water for injection, USP, 2 mL. (See Figure 1 below).

Figure 1

Please read the instructions completely before you begin.



Trelstar is administered via intramuscular injection only under the supervision of a physician. To prepare for injection, two milliliters of sterile water should be drawn up into a needle fitted with a 21-gauge needle and injected into the product vial. Shake the vial well to thoroughly disperse the particles to obtain a uniform suspension and then slowly withdraw the entire contents of the reconstituted suspension into the syringe. The suspension should be administered immediately after reconstitution. When using the Trelstar MIXJECT delivery system, the following illustration details preparation and administration:

(b) (4)

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis' staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division 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.¹

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Trelstar, 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 CDER.

For the proprietary name, Trelstar, DMEPA searches a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Section 2.1.1 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).

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Mode 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. We use the clinical expertise of DMEPA 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. Although our staff typically performs an FDA Prescription Analysis Study for proposed proprietary name reviews, no study was conducted for this review since Triptorelin Pamoate is already marketed as Trelstar Depot and Trelstar LA.

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, DMEPA considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the

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

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

proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, we consider the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

2.1.1 Search Criteria

DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter ‘T’ 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.^{4,5}

To identify drug names that may look similar to Trelstar, 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 (eight letters), capital letters (‘T’), down strokes (none), upstrokes (capital letter ‘t’, l and ‘t’), cross-strokes (‘t’) and dotted letters (none).

Additionally, several letters in Trelstar may be vulnerable to ambiguity when scripted, including the capital letter ‘T’ may appear as capital letter ‘’I’; lower case ‘r’ may appear as a lower case ‘n’, ‘v’ or ‘u’; lower case ‘e’ may appear as lower case ‘l’, ‘r’ or ‘i’; lower letter ‘l’ may appear as lower case letter ‘t’ or ‘e’; lower case letter ‘s’ may appear as lower case letter ‘r’ or ‘a’; lower case ‘t’ may appear lower case ‘l’, ‘i’ or ‘r’; and lower case ‘a’ may appear as lower case ‘o’, ‘c’ or ‘s’. As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Trelstar.

When searching to identify potential names that may sound similar to Trelstar, the DMEPA staff searches for names with similar number of syllables (2), stresses (TREL-star or Trel-STAR), and placement of vowel and consonant sounds. Additionally, there are letters in Trelstar that may be vulnerable to misinterpretation when spoken, including

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

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

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

‘Trel’ may be interpreted as ‘Tel’ and ‘star’ may be misinterpreted as ‘sta’. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered. The Applicant’s intended pronunciation of the proprietary name is Trel-stär.

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 DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Trelstar), the established name (Triptorelin Pamoate), proposed indication (palliative treatment of advanced prostate cancer), strength (3.75 mg, 11.25 mg and 22.5 g), dose/frequency (3.75 mg every four weeks, 11.25 mg every 84 days or 22.5 mg every 24 weeks), route of administration (intramuscular injection) and dosage form (powder for injectable suspension). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

Lastly, the DMEPA staff also considers the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and we provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name, Trelstar, was provided to 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 Trelstar 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 uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the medication error staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

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

The pooled results of the DMEPA 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. As part of the Expert Panel Discussion, the group also provides handwriting samples of the proposed proprietary name along with other look-alike names identified by the panel and the Reviewing Safety Officer.

2.1.2 Comments from the Office of New Drugs

As part of the Division of Medication Error Prevention and Analysis proprietary review process, our staff requests the regulatory Division in the Office of New Drugs responsible for the product to review the proposed proprietary names for comments regarding clinical issues they may have, as well as respond to comments provided by the Division of Drug Marketing, Advertising and Communications evaluation of the name. Additionally, we ask the Division to provide a response to our initial assessment of our Failure Mode and Analysis (FMEA) findings of the proposed proprietary name approximately 45 days before finalizing our review. On February 13, 2009, DMEPA met with the medical review team in the Office of New Drugs, Division of Drug Oncology Products, to discuss these issues and provide input on the Applicant's proposal to name this product 'Trelstar' as well as the Applicant's prior approval requests to change the names of the currently marketed Trelstar Depot and Trelstar LA to 'Trelstar'. DMEPA concerns included the potential for confusion and inadvertent substitution between the three strengths if managed under one 'Trelstar' name as well as the risk of combining strengths to acquire an obtainable dose (i.e. using two 11.25 mg strengths to obtain a 22.5 mg strength dose).

Additionally, DMEPA contacted the Office of New Drug Quality Assessment on March 12, 2009 for their input and comments.

2.1.3 Medication Error Risk Assessment

Since there are already two Triptorelin Pamoate products currently marketed in the United States, Trelstar Depot (3.75 mg) and Trelstar LA (11.25 mg), the Division of Medication Error Prevention and Analysis conducted a search of the Adverse Event Reporting System (AERS) database to determine if there are any medication errors which may be indicative of potential name confusion, product confusion or labeling confusion for the two currently marketed products.

The Division of Medication Error Prevention and Analysis performed a search of the FDA Adverse Event Reporting System (AERS) database on February 3, 2009 using MedRA High Level Group Term (HLGT) "Medication Errors" and Preferred Term (PT) "Pharmaceutical Product Complaint" as search criteria for Reactions. The search criteria used for Products was the active ingredient "Triptorelin Pamoate", the trade names "Trelstar", "Trelstar Depot" and "Trelstar LA", along with the verbatim term "Trelstar%".

The cases were manually reviewed to determine if a medication error occurred. Those cases that did not describe a medication error were excluded from further analysis. The cases that described a medication were categorized by type of error. The Safety Evaluator reviewed the cases within each category to identify factors that contributed to

the medication errors, and to ascertain if these risks might apply to the Trelstar product line.

2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

2.1.4.1 Proprietary Name Risk Assessment

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, the Division 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 Trelstar 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 Trelstar 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 name possesses similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking “Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?” The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the

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

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.

We will object to the use of proposed proprietary name when one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. We identify that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. DMEPA staff identifies a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, World Health Organization, Joint Commission on the Accreditation of Healthcare Organizations and the Institute for Safe Medication Practices, who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, we contend that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the 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, we believe that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

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

Additionally, due to our concerns about potential product strength confusion, DMEPA requested (on January 9, 2009) that the Applicant submit a plan outlining their transition plan for the name change of the two current strengths (3.75 mg-NDA 20-715 and 11.25 mg-NDA 21-288), as well as introduction of the new 'Trelstar' name for the proposed new strength (22.5 mg-NDA 22-437). On January 30, 2009, the Applicant submitted the requested information along with comments regarding the integration of one package insert labeling document for all three strengths. (see Appendix I for Implementation Plan).

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The Division of Medication Error Prevention and Analysis' searches identified twenty-two names with some similarity to the proprietary name, Trelstar: (b) (4), Menostar, Prestara, Relistor, Telintra, Temodar, Tracleer, Travatan, Trecator, Trelibec, Trendar, Trental, Trilafon, Trilean, Trileptal, Trilisa, Trilisate, Trilitron, Vasotec, (b) (4), Trelstar Depot and Trelstar LA.

Nineteen of the twenty-two names were thought to look like Trelstar: (b) (4), Menostar, Prestara, Relistor, Telintra, Temodar, Tracleer, Travatan, Treceptor, Trelibec, Trendar, Trental, Trilafon, Trilean, Trileptal, Trilisa, Trilisate, Trilitron, and Vasotec.

One name, (b) (4), was thought to sound like Trelstar.

Two of the twenty-two names were thought to look and sound like Trelstar: Trelstar Depot and Trelstar LA (although we note that the Applicant has submitted prior approval supplement requests to change these two products to the name ‘Trelstar’ also**).

Additionally, the Division of Medication Error Prevention and Analysis did not identify any United States Adopted Names (USAN) stems in the name Trelstar as of February 3, 2008.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by the staff (see section 3.1.1. above) but did not identify any additional names with similarity to Trelstar.

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

3.1.3 Comments from the Office of New Drugs

On February 13, 2009, DMEPA met with the Division of Drug Oncology Products and discussed the Applicant’s proposal to name the product currently under review, new drug application (NDA 22-437), Trelstar, along with their request to change the currently marketed products, Trelstar Depot and Trelstar LA, to Trelstar. The Division commented on the pending application for the new 22.5 mg strength, stating that this product is a different controlled-release formulation than the 3.75 mg and 11.25 mg strength products. Due to this variation in formulation for the 22.5 mg strength, there is a greater potential for medication error to occur under one ‘Trelstar’ product line name, if strengths are combined to reach an achievable dose (i.e. two 11.25 mg strengths combined to reach a 22.5 mg dose).

On Friday, March 13, 2009, the Division of Oncology Products and the Division of Drug Quality Assessment concurred with DMEPA’s objections to the proposed name, Trelstar. They additionally commented that modifiers for the currently marketed products (LA and Depot) do not intuitively communicate frequency of dosing the health care providers administering the product, and that consideration should be made to the selection of new modifiers for the Trelstar product line that align more intuitively with the frequency of dosing for each of the three strengths.

3.1.4 Medication Error Risk Assessment

Our search of the Adverse Events Reporting System (AERS) yielded a total of six cases, however, none of the cases were deemed relevant to medication errors involving the Trelstar product line. All six cases involved reports of a variety of adverse events including nausea/photophobia/visual disturbance after treatment with Decapeptyl containing same active ingredient, Triptorelin (n=2), depression during clinical trial with other chemotherapy for breast cancer (n=2), unintended pregnancy during treatment with

decreased efficacy (n=1), and foreign report of subcutaneous nodule/neuralgia after incorrect subcutaneous injection after use of Decapeptyl containing the same active ingredient, Triptorelin (n=1).

No relevant cases involving Trelstar name confusion or product confusion involving container labels or carton labeling were retrieved.

3.1.5 Safety Evaluator Risk Assessment

3.1.5.1 Proprietary Name Risk Assessment

Independent searches by the primary Safety Evaluator identified two additional names thought to look like Trelstar: Rifater and Sulster. As such, a total of 24 names were analyzed to determine if the drug names could be confused with Trelstar and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and/or phonetic similarity to Trelstar, and thus determined to present some risk of confusion. Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name Trelstar could potentially be confused with any of the 24 names and lead to medication error. FMEA analysis determined that the name similarity between Trelstar and 22 of the 24 names identified were unlikely to result in medication error. (See Appendices B through H for our evaluation of the 22 names). The FMEA analysis determined that confusion could occur between Trelstar and the currently marketed products, Trelstar LA and Trelstar Depot. Product extension errors are common. However, the Applicant proposes to remove the modifiers 'LA' and 'Depot' and thus, the FMEA indicates confusion can occur (See Appendix I).

The proposed name, Trelstar formulation is unlike that of the 3.75 mg and 11.25 mg strength products. Because of the formulation of the 22.5 mg differs and is designed to release the active ingredient over 24 weeks, strength combinations of the lower strengths should not be used to achieve the 22.5 mg dosage. DMEPA believes that managing all three strengths under the name 'Trelstar' may mislead practitioners to believe the formulations are interchangeable and increase the potential for confusion and inappropriate substitution that would result in medication errors.

3.1.5.2 Applicant Trade Name Implementation Plan

The Applicant's implementation plan included communication and marketing plans for both the currently marketed strengths (3.75 mg and 11.25 mg) designated as 'Phase 1' of the plan, as well as communication and marketing plans for the pending new strength (22.5 mg) designated as 'Phase 2'. The Applicant states in their plan however, that the plans assume that the trade name change for the 3.75 mg and 11.25 mg strengths will be approved prior to the NDA 22-437 for the 22.5 mg strength and they further clarify that if the name change for all three strengths are approved concurrently, the communications and marketing portions of their proposed implementation plan will be combined.

The Phase 1 Communication Plan addresses outreach efforts to communicate the Trelstar name change for the 3.75 mg and 11.25 mg strengths to a wide array of sources.

The Phase 1 Marketing Plan addresses the necessary revisions to product material to effectively revise all printed material for 'Trelstar Depot' and 'Trelstar LA' to the new name, 'Trelstar'. The applicant proposes a 60 day transitional timeframe following FDA approval of the proposed proprietary name, Trelstar for the 3.75 mg and 11.25 mg strengths. The Applicant states that once new literature is complete and distributed, the use of old literature with the 'Trelstar Depot' and 'Trelstar LA' brand names will be discontinued, and the remaining inventory will be destroyed.

Additionally, the Phase 1 Marketing Plan address the revisions of current product packaging and inventory management including package insert labeling, carton labeling and container labels for the Trelstar Depot and Trelstar LA products. The Applicant plans to start production of new packaging and labeling material within 30 days of FDA approval of the prior approval supplement labeling for the 3.75 mg, 11.25 mg and 22.5 mg strengths (to be reviewed separately in OSE Review #2009-18). The Applicant does, however, request that the Agency allow a time window of within 180 days to distribute current packaging with current package inserts in order to utilize existing levels of finished goods inventory while stocking sufficient levels of finished goods inventory with new branded packaging and package insert labeling.

Phase 2 of the implementation plan addresses both communications and marketing plans for the pending new Trelstar 22.5 mg strength. The Phase 2 Communication Plan proposes similar outreach communications to internal and external stakeholders providing notification about the availability of the new 22.5 mg strength. The Applicant plans to execute necessary communications within 30 days of FDA approval.

The Phase 2 Marketing Plan similarly addresses development and distribution of marketing material/literature within 60 days of FDA approval of new drug application (NDA-22-437) along with production of new product packaging and labeling, including package insert labeling, carton labeling and container labels. The Applicant does plan to begin new packaging and labeling production prior to FDA approval to accommodate the limited product levels needed to cover forecasted demand from September 2009 to December 2009. The Applicant plans to start stocking finished goods inventory of Trelstar 22.5 mg within 30 days of FDA approval of the application and plans to begin the commercialization and distribution of Trelstar 22.5 mg to customers within 60 days of FDA approval.

The Applicant further proposes that upon request from the Agency, and subsequent to the approval of new drug application (NDA 22-437) Trelstar 22.5 mg, they would submit prior approval supplement to integrate the three existing package insert labeling (NDA 20-715, 3.75 mg, NDA 21-288, 11.25 mg and NDA 22-437, 22.5 mg) into a combined package insert labeling document for all three strengths. They further explain that the rationale for currently keeping the three package insert labeling documents separate is due to the fact that the 22.5 mg strength is not yet approved and they would like to keep the labeling separate to ensure that any changes made to the 22.5 mg information will not impact the existing marketed product insert labeling.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

The FMEA analysis indicates that the proposed name is vulnerable to name confusion that could lead to medication errors in a clinical practice setting for the currently marketed products, Trelstar LA and Trelstar Depot, if the modifiers 'LA' and 'Depot' are removed as requested by the Applicant. This confusion will occur because the new 22.5 mg strength will not differentiate the proposed product from the currently marketed products. Inappropriate substitution could occur between the 22.5 mg strength and the currently marketed 3.75 mg and 11.25 mg if they are all managed under the single trade name, Trelstar. Clinicians may mistakenly conclude that the three products vary only in their strength and can be used interchangeably and combine smaller strengths to an achievable 22.5 mg dose. Since the 22.5 mg formulation has a different extended-release formulation, such strength combinations would not effectively provide the same extended-release 22.5 mg dose intended for release over a 24 week period. Managing all three products under one 'Trelstar' trade name or naming this product 'Trelstar' alone while retaining the currently marketed proprietary names, creates the potential for product confusion that could lead medication errors such as improper dose administration, wrong product selection or wrong formulation selection.

In conjunction with these safety concerns identified, DMEPA also objects to the Applicant's prior approval supplement name change request to 'Trelstar' for currently marketed Trelstar Depot, new drug application (NDA 20-715, S-018) and Trelstar LA, new drug application (NDA 21-288, S-015). The two currently marketed products, Trelstar Depot and Trelstar LA, are differentiated by their modifiers 'Depot' and 'LA'. Because our medication error search of the AERS database did not retrieve any product strength confusion medication errors for Trelstar Depot or Trelstar LA, it is possible that these modifiers may be providing adequate product distinction that differentiates the two strengths in the clinical setting and should, therefore, be retained.

4.2 APPLICANT TRADE NAME IMPLEMENTATION PLAN

The Applicant's Implementation Plan is based on the approval of the pending new drug application (NDA 22-437) under the proposed name 'Trelstar' and the approval of the two prior approval supplements for new drug applications (NDA 21-288 and NDA 20-715) for the proposed name change to 'Trelstar'. Because DMEPA objects to the proposed proprietary name, Trelstar, for new drug application (NDA 22-437), as well as the proposed 'Trelstar' name change for currently marketed products, Trelstar Depot and Trelstar LA, the Applicant's proposed Implementation Plan is no longer applicable for consideration.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Trelstar, creates safety concerns due to the potential for product strength confusion between the currently marketed 3.75 mg and 11.25 mg strengths, since this new 22.5 mg strength has a different extended-release formulation. Managing all three strengths under

the single trade name ‘Trelstar’ could lead clinicians to conclude that the three products vary only in their strength and can be used interchangeably to combined smaller strengths to an achievable 22.5 mg dose. Since the 22.5 mg formulation has a different extended-release formulation, such strength combinations would not effectively provide the same extended-release 22.5 mg dose intended for release over a 24 week period. Therefore, we object to the use of the proposed proprietary name, Trelstar.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

DMEPA has completed our review of the proposed proprietary name, Trelstar, and have concluded it is not acceptable and have provided comments to the Applicant in Section 6.2. Additionally, in conjunction with our objection to the proposed proprietary name ‘Trelstar’ for new drug application (NDA 22-437), DMEPA plans to submit a separate memorandum to the Division, outlining our objection to Applicant’s prior approval supplement name change request to ‘Trelstar’ for currently marketed Trelstar Depot, new drug application (NDA 20-715, S-018) and Trelstar LA, new drug application (NDA 21-288, S-015) for the reasons outlined above. DDOP comments include recommendations that all three Trelstar products may be better managed under three ‘new’ modifiers that more intuitively align with each product’s frequency of dosing. We would like to meet with you to further discuss your comments, in order to provide appropriate guidance to the Applicant on future name developments for the two products.

6.2 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Trelstar, and have concluded that it is not acceptable for the following reasons:

The 22.5 mg strength has a new extended-release formulation with a mechanism of action that is different from the 3.75 mg and 11.25 mg strengths. Managing all three products under one ‘Trelstar’ trade name or naming this product ‘Trelstar’ alone while retaining the currently marketed proprietary names, creates the potential for product confusion that could lead medication errors such as improper dose administration, wrong product selection or wrong formulation selection. Product confusion and inappropriate substitution could occur between the 22.5 mg strength and the currently marketed 3.75 mg and 11.25 mg strength products. Clinicians may mistakenly conclude that the three products vary only in their strength and can be used interchangeably and combine smaller strengths to an achievable 22.5 mg dose. Since the 22.5 mg formulation has a different extended-release formulation, such strength combinations would not effectively provide the same extended-release 22.5 mg dose intended for release over a 24 week period.

Given these concerns, we recommend:

- a. Contain a modifier that aligns accurately with the product’s clinically proven claims (i.e. Trelstar ‘NEW MODIFIER’). Given that the Trelstar product line is already marketed with two modifiers (LA and Depot) to convey the extended-release nature of the formulation, please provide data that demonstrates that the proposed modifier provides adequate differentiation between the Trelstar products and has a meaning that is consistently and readily understood by healthcare practitioners.

- b. That you submit another proposed proprietary name for the 22.5 mg strength product.

7 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. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in 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:

The Medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. We also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication error staff also 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has led to medication errors. The Medication error staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication error staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, we 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, we also consider a variety of pronunciations that could occur in the English language.

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

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product	<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 communicationNames may look similar

Look-alike		characteristics	when scripted and lead to drug name confusion in written communication
	Orthographic similarity	<p>Similar spelling</p> <p>Length of the name</p> <p>Upstrokes</p> <p>Downstrokes</p> <p>Cross-strokes</p> <p>Dotted letters</p> <p>Ambiguity introduced by scripting letters</p> <p>Overlapping product characteristics</p>	<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	<p>Identical prefix</p> <p>Identical infix</p> <p>Identical suffix</p> <p>Number of syllables</p> <p>Stresses</p> <p>Placement of vowel sounds</p> <p>Placement of consonant sounds</p> <p>Overlapping product characteristics</p>	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Names lacking convincing look-alike or sound-alike similarities to Trelstar

Proprietary Name	Similarity to Trelstar
Vasotec	Look-Alike

Appendix C: Drug names not found in commonly referenced databases

Proprietary Name	Similarity to Trelstar
Trilean	Look-Alike
Trilisa	Look-Alike

Appendix D: Drug names with limited availability in other countries

Proprietary Name	Similarity to Trelstar	Country
Trelibec	Look-Alike	Chile, Germany

Appendix E: Drug names withdrawn or discontinued (No longer available)

Proprietary Name	Similarity to Trelstar	Status
Trendar	Look-Alike	Withdrawn by Agency 1982
Trilitron	Look-Alike	Discontinued 2001 – no generics avail.

Appendix F: Drug names that were past proposed proprietary names**

Proprietary Name	Similarity to Trelstar	Status
(b) (4)	Look-Alike	(b) (4)
(b) (4)	Sound-Alike	(b) (4)

Appendix G: Drug names with no numerical overlap in strength and dose

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Trelstar (Triptorelin Pamoate) for Injectable Suspension		22.5 mg	Inject 2 mL sterile water into vial and shake well; withdraw the entire content of reconstituted suspension into syringe (or using MIXJECT delivery device) and inject intramuscularly administered only under physician supervision. 3.75 mg: Single intramuscular injection every month; 11.25 mg every 84 days in either buttock; 22.5 mg every twenty-four weeks
Menostar (Estradiol)		0.014 mg/24 hour Extended Release Transdermal Patch	Apply patch to skin as prescribed for seven-day dosing interval.
Prestara (Dehydroepiandrosterone {DHEA})		25 mg tablets	50 mg twice daily for adjunctive support of andropause in men 50 mg once daily for treatment of impotence secondary to erectile dysfunction *Orphan drug designation for adjunctive treatment of mild to moderate treatment of systemic lupus (SLE) 200 mg once daily

Relistor (Methylnaltrexone Bromide)		12 mg/0.6 mL Solution for Subcutaneous Injection	8 mg (patients weight 38 kg to 62 kg) or 12 mg (patients weighing 62 kg to 114 kg) administer one dose subcutaneous injection every other day, as needed but no more frequently than one dose every 24-hour period
Temodar (Temozolomide)		5 mg, 20 mg, 100 mg, 250 mg, 140 mg, 180 mg Capsules	Dosage adjusted according to nadir neutrophil and platelet count and calculated based on body surface area (BSA) with varying cycles depending on patient diagnosis (patients with newly diagnosed high grade Glioma 75 mg/m ² ; patients with refractory Anaplastic Astrocytoma 150 mg/m ² .)
Tracleer (Bosentan)		62.5 mg and 125 mg tablets	Initiate dose of 62.5 mg twice daily for four weeks and then increase to maintenance dose of 125 mg twice daily.
Travatan (Travoprost)		0.004 % Ophthalmic Solution	One drop in affected eye(s) once daily in the evening.
Trecator (Ethionamide)		250 mg tablet	Therapy initiated at a dose of 250 mg daily, with gradual titration to optimal doses as tolerated by patient. Usual dose is 15 to 20 mg/kg/day administered once daily
Trental (Pentoxifylline)		400 mg Extended-release tablet	400 mg three times daily
*Trilafon (Perphenazine) *Discontinued but generics available		2 mg, 4 mg, 8 mg and 16 mg Tablets	Dosage individualized and adjusted to severity of condition and response obtained: 4 mg to 8 mg three times daily initially, reduce as possible to minimum effective dosage 8 mg to 16 mg twice daily to three times daily; avoid dosages in excess of 64 mg daily
Trileptal (Oxcarbazepine)		150 mg, 300 mg and 600 mg Tablet 300 mg/5 mL Oral Suspension	Adults Adjunctive therapy: Initiate 600 mg/day given twice a day intervals; may increase by a maximum of 600 mg/day at weekly intervals Conversion to Monotherapy: 600 mg/day given twice daily intervals while simultaneously initiating reduction of the dose of concomitant anti-epileptic drug Initiation Monotherapy: 600 mg/day in twice daily intervals; dose increased by 300 mg/day every third day Pediatric: Ages 4-16: 8 mg/kg to 10 mg/kg Ages 2 to less than 4 years old: dose not to exceed 600 mg/day given in twice daily regimen
Trilisate (Choline Magnesium Trisalicylate)		500 mg, 750 mg or 1000 mg tablets	Adults starting dose 1500 mg given twice daily; may be treated with 3000 mg given once daily at bedtime For mild to moderate pain: 2000 mg to 3000 mg daily in twice daily divided doses
Rifater (Isoniazid, Pyrazinamide and Rifampin)		Isoniazid 50 mg, Pyrazinamide 300 mg and Rifampin 120 mg Tablet	Patients should be given a single daily dose eight one or two hours after a meal: -Patients weight less than 44 kg: Four tablets -45 kg to 54 kg: Five tablets -Greater than 55 kg: Six tablets
Sulster (Prednisolone Sodium Phosphate and Sulfacetamide Sodium)		Prednisolone Sodium Phosphate 0.23 % and Sulfacetamide Sodium 10 % Ophthalmic Eye drops	Instill two drops into affected eye(s) every four hours.

Appendix H: Proposed Names Currently Under Development

Failure Mode: Name confusion	Causes (could be multiple)	Effect
Trelstar (Triptorelin Pamoate) for Injectable Suspension	22.5 mg	Inject 2 mL sterile water into vial and shake well; withdraw the entire content of reconstituted suspension into syringe (or using MIXJECT delivery device) and inject intramuscularly administered only under physician supervision. Single intramuscular injection every month
**Telintra (Ezatiostat Hydrochloride) (Product currently under development with limited product information available)	Orthographic similarities include: Both names begin with the capital letter ‘T’ the beginning of the two names are similar ‘Trel’ and ‘Tel’. Both names have the letter ‘t’ placed in the third from the last letter position.	Orthographic differences and variations in the dosage form minimize the potential for product confusion that could lead to medication error in the clinical practice setting. <i>Rationale:</i> The endings of the two names vary in their letter presentation, ‘tra’ versus ‘tar’. Telintra is currently under development for the treatment of cancer patients in oral and injectable formulations while Trelstar is available only as a injectable suspension for intravenous injection. Dosage form would be specified in physician orders, differentiating the two products.

Appendix I: Potential name confusion with Trelstar Depot and Trelstar LA

Failure Mode: Name confusion	Causes (could be multiple)	Effect
Trelstar (Triptorelin Pamoate) for Injectable Suspension	22.5 mg	Inject 2 mL sterile water into vial and shake well; withdraw the entire content of reconstituted suspension into syringe (or using MIXJECT delivery device) and inject intramuscularly administered only under physician supervision. Single intramuscular injection every month
Trelstar Depot (Triptorelin Pamoate) for Injectable Suspension 3.75 mg	Orthographic and Phonetic Similarities: Same root trade name ‘Trelstar’	Name differentiation through the use of the modifier ‘Depot’** along with variation in strength, usual dose and frequency of administration minimize the potential for medication error occurrence. <i>Rationale:</i> The ‘Depot’** modifier along with the strength (3.75 mg), the dose (3.75 mg) and the frequency of administration (every 4 weeks) differentiate this product from the other Trelstar products. Because the drug is only given in a supervised clinical setting, the strength, dose and the frequency of administration would be included on physician orders, thereby minimizing the potential for product confusion that could lead to medication errors. **The Applicant has submitted a prior approval supplement to change the trade name to ‘Trelstar’ for all strengths. DMEPA plans to recommend that the name change for all Trelstar strengths occur simultaneously to minimize the potential for product confusion.
Trelstar LA (Triptorelin Pamoate) for Injectable Suspension 11.25 mg	Orthographic and Phonetic Similarities: Same root trade name ‘Trelstar’	Name differentiation through the use of the modifier ‘LA’** along with variation in strength, usual dose and frequency of administration minimize the potential for medication error occurrence. <i>Rationale:</i>

		<p>The 'LA' modifier along with the strength (11.25 mg), the dose (11.25 mg) and the frequency of administration (every 84 days) differentiate this product from the other Trelstar products. Because the drug is only given in a supervised clinical setting, the strength, dose and the frequency of administration would be included on physician orders, thereby minimizing the potential for product confusion that could lead to medication errors.</p> <p>**The Applicant has submitted a prior approval supplement to change the trade name to 'Trelstar' for all strengths. DMEPA plans to recommend that the name change for all Trelstar strengths occur simultaneously to minimize the potential for product confusion.</p>
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