CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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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
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	November 27, 2013
Reviewer:	Loretta Holmes, BSN, PharmD Division of Medication Error Prevention and Analysis
Team Leader:	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Orenitram (Treprostinil) Extended-release Tablets 0.125 mg, 0.25 mg, 1 mg, and 2.5 mg
Application Type/Number:	NDA 203496
Applicant:	United Therapeutics Corporation
OSE RCM #:	2013-2111

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CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Orenitram, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A, respectively.

The Division of Medication Error Prevention and Analysis previously reviewed the proposed names (b) (4) (OSE Review 20912-533, dated May 17, 2012) and (b) (4) (OSE Review 2012-1321, dated September 4, 2012) for this NDA and found both names unacceptable.

1.1 BACKGROUND

United Therapeutics is the Applicant for the following products:

- Remodulin (Treprostinil) Injection (NDA 021272), approved on May 21, 2002
- Tyvaso (Treprostinil) Solution for Inhalation (NDA 022387), approved on July 30, 2009

Orenitram (Treprostinil) Extended-release Tablet is the third dosage form for Treprostinil introduced by United Therapeutics for the indication of treatment of Pulmonary Arterial Hypertension (PAH) World Health Organization (WHO) group 1. Remodulin and Tyvaso are considered dual proprietary names since they contain the same active ingredient marketed by the same manufacturer. If granted, Orenitram would be the third proprietary name for the same active ingredient (Treprostinil), for the same indication (PAH), by the same Applicant (United Therapeutics). DMEPA previously evaluated the appropriateness of a third proprietary name. We determined that a third proprietary name is acceptable.

1.2 PRODUCT INFORMATION

The following was provided in the November 27, 2013 submission of product characteristics information. If approved, this will be the first oral formulation of Treprostinil.

Table 1. Orenitram Product Characteristics

Active Ingredient	Treprostinil
Indication of Use	Treatment of pulmonary hypertension (WHO Group 1) to improve exercise capacity.
Route of Administration	Oral
Dosage Form	Extended-release Tablets
Strengths	0.125 mg, 0.25 mg, 1 mg, and 2.5 mg
Dose and Frequency	Take Orenitram with food. Swallow Orenitram intact; use only intact tablets. The recommended starting dose of Orenitram is 0.25 mg twice daily (BID) with food, taken approximately 12 hours apart.

	Increase the dose as tolerated to achieve optimal clinical response. The recommended increment is 0.25 or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID dose increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily with food (TID; approximately 8 hours apart), titrating by increments of 0.125 mg TID. The mean dose in a controlled clinical trial at 12 weeks was 3.4 mg BID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study. *Hepatic impairment:* In patients with mild hepatic impairment (Child Pugh Class A) start at 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days. Avoid use of Orenitram in patients with moderate hepatic impairment (Child Pugh Class B). Orenitram is contraindicated in patients with severe hepatic impairment (Child Pugh Class C). *Concomitant administration with CYP2C8 inhibitors:* When co-administered with strong CYP2C8 inhibitors the initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.
How Supplied	100-count bottles with (b) (4)
Storage	Store at 25°C (77°F); excursions 15°C to 30°C (59°F to 86°F) [See USP controlled room temperature].
Container and Closure System	HDPE bottles with (b) (4)

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Cardiovascular and Renal Products (DCRP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) SEARCH

There is no USAN stem present in the proposed proprietary Orenitram.[1]

[1] USAN stem list searched October 11, 2013.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide the derivation or intended meaning of the name, Orenitram, in their submission. Orenitram is an extended-release formulation comprised of one active ingredient, Treprostinil. The Applicant does not include a modifier with the name (e.g., ER, XR, XL) to convey that Orenitram is an extended-release dosage form.

In OSE Review 2012-1321, dated September 4, 2012, DMEPA evaluated the necessity of having a modifier in the name of this product to convey its extended-release dosage form. We determined a modifier was unnecessary..

2.2.3 FDA Name Simulation Studies

Seventy-eight practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with currently marketed products nor did they appear or sound similar to any currently marketed products or products pending in the pipeline. The written prescription studies indicate the letters "O" and "m" and can be misinterpreted as the letters "A" and "n", respectively. The verbal prescription study indicates that "i" can be misheard as "a". We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). Appendix C contains the results of the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, September 25, 2013 e-mail, the Division of Cardiovascular and Renal Products (DCRP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

The potential letter and letter string variations listed in Appendix B were used to search for names with possible orthographic and phonetic similarity to the proposed proprietary name, Orenitram (Table 1).

Our analysis of the 28 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined all 28 names will not pose a risk for confusion as described in Appendices D through E.

Table 1: Collective List of Potentially Similar Names from the Expert Panel Discussion (EPD) and Primary Safety Evaluator					
Look Similar (n=28)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Arimidex	EPD	Quintabs	EPD	Asenapine	EPD
Omnitrope	EPD	Oratane***	EPD	Acitretin	EPD
Oxandrin	EPD	Orathecin***	EPD	Oxacillin	EPD
Minitran	EPD	Orencia	EPD	Urealac	EPD
Questran	EPD	Quinidine	EPD	Orvaten	EPD
Arestin	EPD	Dronedarone	EPD	Oxsoralen	EPD
Orlaam	EPD	Oratuss	EPD	Prometrium	EPD
Uretron	EPD	Quinidex	EPD	Accutane	EPD
Quenalin	EPD	Carmustine	EPD	Granisetron	Primary Safety Evaluator
(b) (4) ***	Primary Safety Evaluator				

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on November 5, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Cardiovascular and Renal Products on November 5, 2013, they stated no additional concerns with the proposed proprietary name, Orenitram.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Cherye Milburn, OSE Project Manager, at 301-796-2084.

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3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Orenitram, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your November 27, 2013 submission are altered, the name must be resubmitted for review.

4 REFERENCES

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

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

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

   POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. 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.

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

   Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products. This database also lists the orphan drugs.

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

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

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

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

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

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

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

   USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)***

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

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

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

10. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

11. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

12. ***Red Book (www.thomsonhc.com/home/dispatch)***

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

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

    Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

14. ***Medical Abbreviations (www.medilexicon.com)***

    Medical Abbreviations dictionary contains commonly used medical abbreviations and their definitions.

15. ***CVS/Pharmacy (www.CVS.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

16. ***Walgreens (www.walgreens.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

17. ***Rx List (www.rxlist.com)***

    RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

18. Dogpile (www.dogpile.com)

Dogpile is a Metasearch engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [2]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

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

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

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

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

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA 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, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Simulation Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[4] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

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

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?"***

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

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

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

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name may be confusing, misleading, cause or contribute to medication errors.

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

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

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

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

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

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Orenitram	Scripted May Appear as	Spoken May Be Interpreted as
Upper Case 'O'	A, C, D, G, Q, U, V	Any vowel
lower case 'o'	a, c, e, u, v	Any vowel
lower case 'r'	c, i, s, n, e, v	
lower case 'e'	a, c, i, l, o, p, r	Any vowel
lower case 'n'	m, u, x, r, h, s	dn, gn, kn, mn, pn
lower case 'i'	e, l, j	Any vowel
lower case 't'	r, f, x, A	d
lower case 'r'	r, s, n, e, v	
lower case 'a'	el, ci, cl, d, e, o, u	Any Vowel
lower case 'm'	rn, nn, n, v, w, wi, vi, onc, z, rv, rr, nr, in	n
Letter Strings		
re	u	
en	m, w	
ni	m, w, in	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Orenitram Study (Conducted on February 21, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Inpatient Medication Order: Orenitram 0.5mg po twice a day	Orenitram 0.25 mg Take 1 tablet by mouth twice daily Disp. #60
Outpatient Prescription: Orenitram 0.25mg 1 tab po BID #60	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

	198 People Received Study
	78 People Responded

Study Name: Orenitram

Total	32	20	26	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
ARENITRAM	0	0	1	1
ARENITRAN	0	0	1	1
GRANITRAM	0	0	1	1
OREITRAM	1	0	0	1
ORENATRAM	0	9	0	9
ORENATRAN	0	2	0	2
ORENETRAN	0	1	0	1
ORENITRAIN	0	0	7	7
ORENITRAM	28	0	12	40
ORENITRAN	3	0	4	7

ORENOTRAM	0	1	0	1
ORENTRIUM	0	1	0	1
ORINATRAM	0	3	0	3
ORINITRAM	0	1	0	1
ORINITRAN	0	1	0	1
ORINOTRAM	0	1	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Drug Name	Active Ingredient	Similarity to Orenitram	Failure preventions
1.	Omnitrope	Somatropin	Look	The pair have sufficient orthographic differences.
2.	Orlaam	Levomethadyl Acetate HCl	Look	The pair have sufficient orthographic differences.
3.	Quenalin	Diphenhydramine HCl	Look	The pair have sufficient orthographic differences.
4.	Carmustine	Carmustine	Look	The pair have sufficient orthographic differences.
5.	Orathecin***	Rubitecan	Look	The pair have sufficient orthographic differences.
6.	Quintabs	Multiple vitamins	Look	The pair have sufficient orthographic differences.
7.	Dronedarone	Dronedarone HCl	Look	The pair have sufficient orthographic differences.
8.	Oratuss	Carbetapentane Citrate and Guaifenesin	Look	The pair have sufficient orthographic differences.
9.	Prometrium	Progesterone	Look	The pair have sufficient orthographic differences.
10.	Accutane	Isotretinoin	Look	The pair have sufficient orthographic differences.
11.	Asenapine	Asenapine Maleate	Look	The pair have sufficient orthographic differences.
12.	Acitretin	Acitretin	Look	The pair have sufficient orthographic differences.
13.	Oxacillin	Oxacillin Sodium	Look	The pair have sufficient orthographic differences.

No.	Drug Name	Active Ingredient	Similarity to Orenitram	Failure preventions
14.	Urealac	Urea	Look	The pair have sufficient orthographic differences.
15.	Oxsoralen	Methoxalen	Look	The pair have sufficient orthographic differences.
16.	Arestin	Minocycline	Look	The pair have sufficient orthographic differences.
17.	Oratane***	Isotretinoin	Look	This proposed name was found unacceptable in OSE Review 2009-2230. The NDA was approved under the name Myorisan.
18.	(b) (4)		Look	This proposed name was found unacceptable in OSE Review 2007-696. The product is currently marketed under the name Lovaza.

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Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

	Proposed name: **Orenitram (Treprostinil) Extended-release Tablets**	**Strengths:** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**Usual Dose: The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **Hepatic impairment: In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **Concomitant administration with CYP2C8 inhibitors: The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
19.	Arimidex (Anastrozole) Tablets Strength: 1 mg Dosage: 1 mg orally once daily	Orthographic: The beginning letter strings "Oreni" vs. "Arimi" look similar when written. Strength, Dose, Route of Administration: Both products are administered orally and overlap with a 1 mg dose and strength.	Orthographic: The suffixes "tram" and "dex" look different when written.

	Proposed name: **Orenitram (Treprostinil) Extended-release Tablets**	**Strengths:** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**Usual Dose: The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **Hepatic impairment: In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **Concomitant administration with CYP2C8 inhibitors: The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
20.	Oxandrin (Oxandrolone) Tablets Strengths: 2.5 mg and 10 mg Dosage: Total daily dose of 2.5 mg to 20 mg; total daily dose may be divided into twice daily, three times per day, or four times per day administration	Orthographic: Both names begin with the letter "O". The infix letters "en" vs. "an" look similar when written. Strength: The products have overlapping strengths (2.5 mg) and numerical similarity in strength (1 mg vs. 10 mg). Frequency of Administration, Route of Administration, and Dosage Form: Both products are tablets and can be administered orally two or three times per day.	Orthographic: The second position letters "r" vs. "x" look different when written. The letter "i" follows the letter "n" in Orenitram whereas the letter "d" follows the letter "n" in Oxandrin. The letter "t" in Orenitram has a cross-stroke which helps to differentiate the names.

	Proposed name: **Orenitram (Treprostinil) Extended-release Tablets**	**Strengths:** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**Usual Dose: The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **Hepatic impairment: In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **Concomitant administration with CYP2C8 inhibitors: The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
21.	Questran (Cholestyramine) Powder Strength: 4 g per packet or scoop Dosage: 4 g (1 packet or scoop) to 8 g (2 packets or scoops) orally twice daily	Orthographic: The beginning letters "O" vs. "Q" look similar when written. The suffixes "tram" vs. "tran" look nearly identical when written. Route and Frequency of Administration: Both products are administered orally twice daily. Dose: The products have numerical overlap in dose (1 mg vs. 1 packet or 1 scoop)	Orthographic: The infix letters "ni" vs. "es" look different when written.

	Proposed name: **Orenitram (Treprostinil) Extended-release Tablets**	**Strengths:** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**Usual Dose: The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **Hepatic impairment: In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **Concomitant administration with CYP2C8 inhibitors: The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
22.	Uretron (b) (4) Tablets Dosage: 2 tablets orally four times per day	Orthographic: The beginning letters "Ore" vs. "Ure" and the suffixes "tram" vs. "tron" look similar when written. Dose: The products have numerical overlap in dose (2 mg vs. 2 tablets). Dosage Form and Route of Administration: Both products are orally administered tablets.	Orthographic: Orenitram contains the infix letters "ni" which lengthens the infix and helps to differentiate the names.

	<u>Proposed name:</u> **Orenitram (Treprostinil) Extended-release Tablets**	**<u>Strengths:</u>** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**<u>Usual Dose:</u> The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **<u>Hepatic impairment:</u> In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **<u>Concomitant administration with CYP2C8 inhibitors:</u> The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
23.	Orencia (Abatacept) Injection for Injection <u>Strength:</u> *Injection:* 125 mg/1 mL syringe *for Injection*: 250 mg per vial <u>Dosage:</u> *Adults:* 500 mg, 750 mg, or 1 g intravenously every 2 weeks for 3 doses then every 4 weeks; 125 mg subcutaneously once weekly *6 to 17 years of age:* Less than 75 kg: 10 mg/kg intravenously 75 kg or more: Same as adult intravenous dosing	<u>Orthographic:</u> Both names begin with the letter string "Oren". <u>Strength:</u> The products have numerical similarity in strength (0.125 mg vs. 125 mg; 0.25 mg or 2.5 mg vs. 250 mg); There is also numerical overlap in strength between 1 mg and 1 g. <u>Dose:</u> The products have numerical similarity in dose (1.25 mg vs. 125 mg; 0.25 mg or 2.5 mg vs. 250 mg)	<u>Orthographic:</u> The letter strings "itram" vs. "cia" look different. <u>Frequency of Administration:</u> Twice daily or three times per day vs. once weekly, every 2 weeks, or every 4 weeks <u>Route of Administration:</u> Oral vs. intravenously or subcutaneously

	Proposed name: **Orenitram (Treprostinil) Extended-release Tablets**	**Strengths:** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**Usual Dose: The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **Hepatic impairment: In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **Concomitant administration with CYP2C8 inhibitors: The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
24.	Orvaten (Midodrine HCl) Tablets Strengths: 2.5 mg, 5 mg, and 10 mg Dosage: 2.5 mg to 10 mg orally three times per day	Orthographic: Both names begin with the letters "Or" and contain the upstroke letter "t". Strength: The products have an overlapping strength (2.5 mg). Dose and Frequency of Administration: The products have overlapping doses (2.5 mg, 5 mg, 10 mg) and can be administered three times per day	Orthographic: The infix letters "eni" vs. "va" look different when written. The letter "r" follows the letter "t" in Orenitram which makes the suffix "tram" vs. "tran" appear longer in length which helps to differentiate the names.

	<u>Proposed name:</u> **Orenitram (Treprostinil) Extended-release Tablets**	**<u>Strengths:</u>** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**<u>Usual Dose:</u> The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **<u>Hepatic impairment:</u> In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **<u>Concomitant administration with CYP2C8 inhibitors:</u> The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
25.	Granisetron Tablets Oral Solution Injection Transdermal Patch <u>Strengths</u>: *Tablets:* 1 mg *Solution:* 2 mg/10 mL *Injection:* 0.1 mg/mL and 1 mg/mL *Transdermal Patch:* 3.1 mg/24 hours <u>Dosage:</u> *Oral:* 2 mg once daily or 1 mg twice daily on chemo days *Intravenous:* 10 mcg/kg 30 minutes before chemo *Transdermal Patch:* Apply 1 patch 24 to 48 hours prior to chemo and wear up to 7 days	<u>Orthographic:</u> The beginning letters "Oreni" vs. "Grani" look similar when written. The suffixes "tram" vs. "tron" look similar when written. <u>Strength and Dose:</u> The products have an overlapping strength (1 mg) and doses (1 mg and 2 mg). <u>Route of Administration and Frequency of Administration:</u> Both products can be administered orally twice daily.	<u>Orthographic:</u> Granisetron contains the infix letters "se" which helps to differentiate the names due to lengthening of the infix.

	Proposed name: **Orenitram (Treprostinil) Extended-release Tablets**	**Strengths:** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**Usual Dose: The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **Hepatic impairment: In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **Concomitant administration with CYP2C8 inhibitors: The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
26.	Quinidex (Quinidine Sulfate) Extended-release Tablets Strength: 300 mg Dosage: Begin with 300 mg orally every 8 to 12 hours. The dose may be cautiously raised if needed. There are no well-described maximum doses for the approved indications according to the prescribing information. Quinidex was discontinued in 2004; however, similar products are currently marketed.	Orthographic: The beginning letters "O" vs. "Q" and the infix letters "eni" vs. "ini" look similar when written. Dose: The products have numerical overlap in dose (1 mg vs. 1 tablet) Dosage form, Route of Administration and Frequency of Administration: Both products are oral tablets that can be administered twice daily or three times per day.	Orthographic: The infix letters "r" vs. "u" look different. The suffixes "tram" vs. "dex" look different.

	Proposed name: **Orenitram (Treprostinil) Extended-release Tablets**	**Strengths:** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**Usual Dose: The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **Hepatic impairment: In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **Concomitant administration with CYP2C8 inhibitors: The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
27.	Minitran (Nitroglycerin) Transdermal Patch Strengths: 0.1 mg/hr, 0.2 mg/hr, 0.4 mg/hr, and 0.6 mg/hr Dosage: Initial: 0.2 mg/hr to 0.4 mg/hr transdermally for 12 to 14 hours daily. Titrate dose to response. There is no well-established maximum dose for the approved indication according to the prescribing information.	Orthographic: The letter strings "enitram" vs. "initran" look similar when written. Strength: There is numerical similarity between the doses and strengths of the products (1 mg vs. 0.1 mg/hr).	Orthographic: The beginning letters "Or" vs. "M" look different.

	<u>Proposed name:</u> **Orenitram (Treprostinil) Extended-release Tablets**	**<u>Strengths:</u>** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**<u>Usual Dose:</u> The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **<u>Hepatic impairment:</u> In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **<u>Concomitant administration with CYP2C8 inhibitors:</u> The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
28.	Quinidine (Quinidine Sulfate) (Quinidine Gluconate) *Quinidine Sulfate Tablets:* 200 mg and 300 mg *Quinidine Sulfate Extended-release Tablets:* 300 mg *Quinidine Gluconate: Extended-release Tablets:* 324 mg *Quinidine Gluconate Injection:* 80 mg/mL <u>Dosage:</u> There are no well-established maximum doses for the approved indications according to the prescribing information *Quinidine Sulfate Tablets:* 400 mg orally every 6 hours; dose may be increased cautiously if needed.	<u>Orthographic:</u> The beginning letters "O" vs. "Q" and the infix letters "eni" vs. "ini" look similar when written. <u>Dose:</u> The products have numerical overlap in dose (1 mg vs. 1 tablet) <u>Dosage Form, Route of Administration, and Frequency of Administration:</u> The products are available in tablet dosage forms and can be administered orally twice daily or three times per day.	<u>Orthographic:</u> The infix letters "r" vs. "u" look different. The suffixes "tram" vs. "dine" look different.

	<u>Proposed name:</u> **Orenitram (Treprostinil) Extended-release Tablets**	**<u>Strengths:</u>** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**<u>Usual Dose:</u> The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **<u>Hepatic impairment:</u> In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **<u>Concomitant administration with CYP2C8 inhibitors:</u> The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
	<u>Quinidine Cont'd</u> *Quinidine Sulfate Extended-release Tablets:* Begin with 300 mg orally every 8 to 12 hours. The dose may be cautiously raised if needed. <u>Quinidine Sulfate Extended-release Tablets:</u> 2 tablets orally every 8 hours, the dose if then cautiously increased if needed 1 tablet every 8 hours for 2 days, then 2 tablets every 12 hours for 2 days, then 2 tablets every 8 hours for up to 4 days *Quinidine Gluconate Injection:* Loading: 24 mg/kg of Quinidine Gluconate in 250 mL of normal saline infused intravenously over 4 hours.		

	<u>Proposed name:</u> **Orenitram (Treprostinil) Extended-release Tablets**	**<u>Strengths:</u>** **0.125 mg, 0.25 mg, 1 mg, and 2.5 mg**	**<u>Usual Dose:</u> The recommended starting dose is 0.25 mg twice daily. Increase the dose as tolerated in increments of 0.25 mg or 0.5 mg BID every 3 to 4 days. If 0.25 mg BID increments are not tolerated consider titrating slower. The total daily dose can be divided and given three times daily (TID), titrating by increments of 0.125 mg TID. Maximum doses studied were 12 mg BID in the 12-week blinded study and up to 21 mg BID in an open-label long-term study.** **<u>Hepatic impairment:</u> In patients with mild hepatic impairment (Child Pugh Class A) start with 0.125 mg BID with dose increments every 3 to 4 days.** **<u>Concomitant administration with CYP2C8 inhibitors:</u> The initial dose is 0.125 mg BID with 0.125 mg BID dose increments every 3 to 4 days.**
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
	<u>Quinidine Cont'd</u> Then, 12 mg/kg of infused over 4 hours every 8 hours, starting 8 hours after the beginning of the loading dose. 10 mg/kg in approximately 5 mL/kg of normal saline over 1 to 2 hours. Then, a maintenance infusion of 20 mcg/kg/min. Less than 5 mg/kg, to as much as 10 mg/kg, no faster than 0.25 mg/kg/min.		

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/s/

LORETTA HOLMES
11/29/2013

IRENE Z CHAN
11/29/2013

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	September 4, 2012
Reviewer:	Irene Z Chan, PharmD, BCPS, Team Leader Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh, Division Director Division of Medication Error Prevention and Analysis
Drug Name and Strength(s):	(b) (4) (Treprostinil) Extended-release Tablets 0.125 mg, 0.25 mg, (b) (4), 1 mg, and 2.5 mg
Application Type/Number:	NDA 203496
Applicant/Sponsor:	United Therapeutics
OSE RCM #:	2012-1321

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IRENE Z CHAN
09/04/2012

CAROL A HOLQUIST
09/04/2012

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	May 17, 2012
Reviewer(s):	Ray Ford, RPh, Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader	Irene Z Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Division Director	Kellie Taylor, PharmD, M. S. Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh, Division Director Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s):	(b) (4) (Treprostinil Diethanolamine) Extended-release Tablets 0.125 mg, 0.25 mg, (b) (4) 1 mg, and 2.5 mg
Application Type/Number:	NDA 203496
Applicant/Sponsor:	United Therapeutics
OSE RCM #:	2012-533

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05/17/2012

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05/17/2012

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05/18/2012

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