# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 203496Orig1s000

# 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

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| Date: | November 27, 2013 |
| Reviewer: | Loretta Holmes, BSN, PharmD<br>Division of Medication Error Prevention and Analysis |
| Team Leader: | Irene Z. Chan, PharmD, BCPS<br>Division of Medication Error Prevention and Analysis |
| Drug Name and Strength: | Orenitram (Treprostinil) Extended-release Tablets<br>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 |

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

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# 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**

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| **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.<br>The recommended starting dose of Orenitram is 0.25 mg twice daily (BID) with food, taken approximately 12 hours apart. |

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| | 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.<br><br>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.<br><br>*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).<br><br>*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.

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