



NDA 203496/S-006

SUPPLEMENT APPROVAL

United Therapeutics Corp.
Attention: Nicole Wilkerson
Regulatory Affairs Manager
55 TW Alexander Drive
PO Box 14186
Research Triangle Park, NC 27709

Dear Ms. Wilkerson:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 1, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Orenitram (treprostinil) 0.125 mg, 0.25 mg, 1 mg, 2.5 mg and 5 mg Extended Release Tablets.

We acknowledge receipt of your amendments dated October 21 and December 7, 2016.

This supplemental new drug application provides for the following revisions to the approved labeling for Orenitram (additions are shown as underlined text and deletions are shown as strikethrough text):

1. Under **ADVERSE REACTIONS**, the following section was added:

6.2 Post-Marketing Experience

The following adverse reactions have been identified during postapproval use of Orenitram: dizziness, dyspepsia, vomiting, myalgia, and arthralgia. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

2. The revision date was updated.

There are no other changes from the last approved package insert and patient package insert.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of

labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call:

Lori Anne Wachter, RN, BSN, RAC
Regulatory Project Manager for Safety
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

MARY R SOUTHWORTH
01/24/2017