DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203496/S-007

SUPPLEMENT APPROVAL

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

Dear Ms. Wilkerson:

Please refer to your Supplemental New Drug Application (sNDA) dated and received march 27, 2017, 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 also refer to our Approval Letter dated June 7, 2017. The approved labeling was not appended to the June 7th letter. This letter corrects that error and supersedes the June 7, 2017 Approval letter. The date of approval will remain June 7, 2017.

This supplemental new drug application provides for revisions to the approved Patient Package Insert as follows (additions are shown as underlined text and deletions are shown as ~~strikethrough~~ text):

1. Under **What are the possible side effects of Orenitram?,** the following text was added/deleted:

   The following (b) (4) side effects have also been (b) (4) observed in patients taking Orenitram (b) (4) after (b) (4) approval (b) (4): dizziness, indigestion, vomiting, muscle pain, and joint pain. (b) (4) (b) (4)

2. The revision date was updated.

APPROVAL & LABELING

We have completed our review of this supplemental application 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 patient 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 include 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
06/07/2017