



NDA 21272/S-015

SUPPLEMENT APPROVAL

United Therapeutics Corporation
Attention: Mr. Dean Bunce
EVP, Regulatory Affairs and Compliance
55 T.W. Alexander Drive
PO Box 14186
Research Triangle Park, NC 27709

Dear Mr. Bunce:

Please refer to your supplemental New Drug Application (sNDA) dated December 17, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Remodulin (treprostinil) 1, 2.5, 5, and 10 mg/mL Injection.

We also acknowledge receipt of your amendment dated January 28, 2011.

This Prior Approval sNDA provides for the following revisions to the labeling for Remodulin (treprostinil).

HIGHLIGHTS OF PRESCRIBING INFORMATION

1. Under the first bullet in **INDICATIONS AND USAGE**, revise the following text

FROM

Remodulin is a prostacyclin vasodilator indicated for:

- Treatment of pulmonary arterial hypertension (PAH) in patients with NYHA Class II-IV symptoms, to diminish symptoms associated with exercise (1.1)

TO

Remodulin is a prostacyclin vasodilator indicated for:

- Treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-

pulmonary shunts (23%), or PAH associated with connective tissue diseases (19%) (1.1)

Full Prescribing Information

2. In section 1.1 of **INDICATIONS AND USAGE**, revise the following text

FROM

1.1 Pulmonary Arterial Hypertension in Patients with NYHA Class II-IV Symptoms

Remodulin is indicated for the treatment of pulmonary arterial hypertension in patients with NYHA Class II-IV symptoms [*see Clinical Studies (14.1)*] to diminish symptoms associated with exercise. It may be administered as a continuous subcutaneous infusion or continuous intravenous infusion; however, because of the risks associated with chronic indwelling central venous catheters, including serious blood stream infections, continuous intravenous infusion should be reserved for patients who are intolerant of the subcutaneous route, or in whom these risks are considered warranted.

TO

1.1 Pulmonary Arterial Hypertension

Remodulin is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary shunts (23%), or PAH associated with connective tissue diseases (19%) [*see Clinical Studies (14.1)*].

It may be administered as a continuous subcutaneous infusion or continuous intravenous infusion; however, because of the risks associated with chronic indwelling central venous catheters, including serious blood stream infections, continuous intravenous infusion should be reserved for patients who are intolerant of the subcutaneous route, or in whom these risks are considered warranted.

Note that minor labeling revisions were made in section 14 of the labeling (**CLINICAL STUDIES**) to be consistent with the revisions made in section 1 (**INDICATIONS AND USAGE**).

3. In section 14.1 of **CLINICAL STUDIES**, revise the following text

FROM

Two 12-week, multicenter, randomized, double-blind studies compared continuous subcutaneous infusion of Remodulin to placebo in a total of 470 patients with NYHA Class II-IV pulmonary arterial hypertension (PAH). PAH was primary in 58% of patients, associated with collagen vascular disease in 19%, and the result of congenital left to right shunts in 23%.

TO

Two 12-week, multicenter, randomized, double-blind studies compared continuous subcutaneous infusion of Remodulin to placebo in a total of 470 patients with NYHA Class II (11%), III (81%), or IV (7%) pulmonary arterial hypertension (PAH). PAH was idiopathic/heritable in 58% of patients, associated with connective tissue diseases in 19%, and the result of congenital systemic-to-pulmonary shunts in 23%.

We note that you also revised the manufacturer information from “Remodulin manufactured by Baxter Pharmaceutical Solutions LLC” to “Remodulin manufactured for United Therapeutics Corp.”

We have completed our review of this supplemental application, as amended. 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, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert, Medication Guide) and include the labeling changes proposed in any pending “Changes Being Effected” (CBE) supplements. 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 for this NDA, including pending “Changes Being Effected” (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.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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 Dan Brum, PharmD, BCPS, RAC, Regulatory Project Manager, at (301)796-0578.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Package Insert

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

/s/

NORMAN L STOCKBRIDGE
02/08/2011