CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-272

CHEMISTRY REVIEW(S)

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-272 **DATE REVIEWED:** 05/17/02

REVIEW #: 03 **REVIEWER:** JV Advani

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
PRE-CMC submission	11-Aug-00	14-Aug-00	15-Aug-00
AMENDMENT (BC)	18-Sep-00	19-Sep-00	20-Sep-00
ORIGINAL SUBMISSION	16-Oct-00	18-Oct-00	19-Oct-00
AMENDMENT (BC)	04-Dec-00	05-Dec-00	12-Dec-00
AMENDMENT (BC)	22-Dec-00	29-Dec-00	08-Jan-01
AMENDMENT (N-BL)	16-Aug-01 & 2 & 21-Feb-02		

Letter dated November 1, 2001 – Non-proprietary name information

NAME & ADDRESS OF APPLICANT: United Therapeutics Corporation
P.O. Box 14186
Research Triangle Park, NC 27709

DRUG PRODUCT NAME

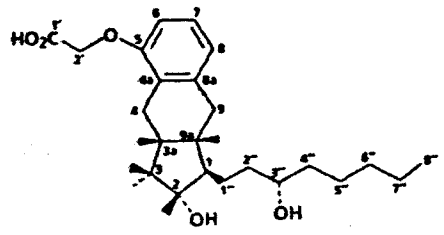
Proprietary:	Remodulin
Established:	Treprostinil sodium
Code Name/#:	UT-15, LRX-15, 15AU81, BW A15AU, U-62,840
Chem.Type/Ther.Class:	1 P
CAS Registry Number	81846-19-7
PHARMACOL. CATEGORY/INDICATION:	Pulmonary Arterial Hypertension
DOSAGE FORM:	Injection
STRENGTHS:	1.0, 2.5, 5.0, and 10.0 mg/mL
ROUTE OF ADMINISTRATION:	Subcutaneous injection
Rx/OTC:	_x_ Rx ___ OTC
PATENT STATUS:	U.S. Patent pending
SPECIAL PRODUCTS:	___ Yes _x_ No

(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

STRUCTURAL FORMULA, CHEMICAL NAME, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Names:

[[(1R,2R,3aS,9aS)-2,3,3a,4,9,9a-hexahydro-2-hydroxy-1-[(3S)-3-hydroxyoctyl]-1H-benz[f]inden-5-yl]oxy]acetic acid monosodium salt



Na^+

Molecular Formula $C_{23}H_{33}NaO_5$ **Molecular weight** 412.49

SUPPORTING DOCUMENTS:

Type/Number	Subject	Holder	Status	Review Date	Letter Date

Material technical data sheets for Type I USP 20 mL Glass is provided. Refer Vol.1.3, pp. 854-877.

RELATED DOCUMENTS (if applicable):

(Submission of 5/95 for UT-15 Injection)

CONSULTS: Microbiology: Micro deficiencies have been resolved. Micro data is acceptable. Microbiologist recommends approval.

REMARKS:

UT-15 Injection is a tricyclic benzindene analog of prostacycline (PGI2) with potent pulmonary and systemic vasodilatory and platelet anti-aggregatory actions in vitro and in vivo. Unlike Flolan (epoprostenol sodium), which must be delivered by continuous intravenous infusion, UT-15 has sufficient chemical stability to allow for subcutaneous administration, offering patients and clinicians an alternate therapeutic route of administration.

All strengths (containing 1.0 mg, 2.5 mg, 5.0 mL and 10.0 mg treprostinol per mL), of UT-15 Injection, is packaged in Type I USP 20 mL . The 20 mL vial is sealed with

The differ in color for product identification.

An EER for establishments was requested on 08/18/00. Overall recommendation for all sites is ACCEPTABLE

Mr. Edward Fromm (PM) sent the labeling and package information provided by firm (in vol.2.9) to current Labeling committee OPDRA for their review. OPDRA review and recommendations are received. Uniprost is not acceptable but Remodulin proprietary name is acceptable.

Expiration date months is proposed when stored at 25°C for the 1.0 mg/mL, 2.5 mg/mL, and 5.0 mg/mL, and expiration date of months for 10-mg/mL strength. Proposed expiration periods will be reviewed when the updated stability data is received from the applicant.

Statistical analysis: Firm has performed the linear regression analysis at 25°C on potency data for lots stored in proposed commercial packaging.

Methods validation will be requested to be performed by 2 district laboratories.

The information submitted in this submission has been previously reviewed under and its amendments.

Firm in letter of November 1, 2001, has indicated that USAN has adopted on July 25, 2001, treprostinil sodium as the non-proprietary name for Remodulin Injection.

CONCLUSIONS & RECOMMENDATIONS: There have been no other changes in chemistry since last review dated 03/06/01. This NDA is satisfactory as far a chemistry is concerned.

Copy of statement on USAN adopted non proprietary name TREPROSTINIL SODIUM is attached with this review.

JV Advani, Review Chemist

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

/s/

J. V. Advani
5/17/02 04:35:47 PM
CHEMIST

Kasturi Srinivasachar
5/17/02 05:10:55 PM
CHEMIST

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-272 **DATE REVIEWED:** 03/06/01

REVIEW #: 02 **REVIEWER:** JV Advani

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL SUBMISSION	16-Oct-00	18-Oct-00	19-Oct-00
AMENDMENT (BC)	23-Feb-01	26-Feb-01	27-Feb-01
AMENDMENT (BL)	26-Feb-01	27-Feb-01	28-Feb-01
AMENDMENT (N-BC)	28-Feb-01	01-Mar-01	01-Mar-01
AMENDMENT (N-BC)	01-Mar-01	02-Mar-01	02-Mar-01

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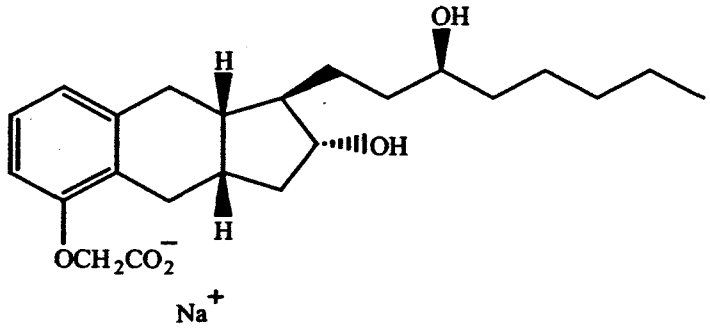

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