SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	COSTA RICA	11	JAN	1957	68 Years	Female	46.00 kg	13	JUL	2025

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [LOWER LEVEL TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Pulmonary arterial hypertension [Pulmonary arterial hypertension]
Fainted [Faint]
Cyanosis, blueish color [cyanotic] [Cyanosis]

Case Description: This Costa Rica case is a solicited report received on 14 Jul 2025, from a nurse from a patient support program via Ferrer. This 68-year-old, 46 kg, female patient began therapy with Remodulin (treprostinil sodium, concentration 5.0 mg/ml), on 24 Sep 2024 for an unknown indication.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 13-JUL-2025
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ OTHER

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Treprostinil sodium (SQ) (TREPROSTINIL SODIUM) Injection, 5.0 mg/ml
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) UNK [0.009 (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous use

17. INDICATION(S) FOR USE
#1) Drug use for unknown indication (Produ
(Continued on Additional Information Page)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2017 to Ongoing	Current Condition diagnosed 8 years ago	
2014 to Ongoing	Current Condition diagnosed 8 years ago	Systemic sclerosis (Systemic scleroderma)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
United Therapeutics
55 T W Alexander Drive, P.O. Box 14186
Research Triangle Park, NC 27709 UNITED STATES
Phone: 1 (919) 485-8350

26. REMARKS
World Wide #: CR-UNITED THERAPEUTICS-UNT-2025-024465
Study ID: PSP_Remodulin_043

24b. MFR CONTROL NO.
UNT-2025-024465

24c. DATE RECEIVED BY MANUFACTURER
23-JUL-2025

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
31-JUL-2025

25a. REPORT TYPE
☐ INITIAL ☒ FOLLOWUP: 1

25b. NAME AND ADDRESS OF REPORTER
COSTA RICA
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
(Continued on Additional Information Page)

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient's dose was unknown [0.00975 mg/ml], continuous via subcutaneous (SQ) route. On 13 Jul 2025, 9 months and 20 days after initiating SQ Remodulin, when the patient was at home, she was accompanied by her husband who helped her go to the bathroom to micturate. However, suddenly, she fainted (syncope, medically significant), and her husband had observed her with a blueish color [cyanotic]; presented with cyanosis. Later, she did not recover from the event and was declared dead (death and medically significant) at 3:00 a.m. The cause of death was not provided, and it was unknown if an autopsy was performed.

Relevant medical history included: pulmonary hypertension [diagnosed 8 years ago], systemic sclerosis, and allergic rhinitis.

Action taken with SQ Remodulin was not applicable for the event of death. Action taken with SQ Remodulin was not reported for the events of syncope and cyanosis. The outcome of syncope and cyanosis was not resolved.

The reporter assessed the causal relationship between the SQ Remodulin, and the events of death, syncope, and cyanosis as not related.

Follow-up information was received on 23 Jul 2025 as a query response via Ferrer.

Relevant medical history was updated to pulmonary arterial hypertension from pulmonary hypertension. Follow up report clarified cause of the death as pulmonary arterial hypertension. Thus, the event of death was updated to pulmonary arterial hypertension (medically significant). The autopsy was not performed. Action taken with SQ Remodulin was not applicable for the event of pulmonary arterial hypertension. The outcome of pulmonary arterial hypertension was fatal.

The reporter assessed the causal relationship between the SQ Remodulin, and the event of pulmonary arterial hypertension as not related.

Case Comment/Senders Comment: The company has assessed the serious adverse events of pulmonary arterial hypertension and syncope as not related to SQ treprostinil. Considering the elderly age of the patient and the long history of underlying pulmonary hypertension of about 8 years, the events were likely related to the underlying PAH. The reported event of pulmonary arterial hypertension was consistent with the chronic and progressive illness of underlying PAH. The reduced blood flow through lungs in PAH results in impaired gas exchange, ventilation perfusion mismatch, reduced diffusing capacity and admixture of mixed venous blood with low oxygen saturation triggers hypoxaemia which coupled with cerebral hypoperfusion leading to cerebral hypoxia likely led to development of syncope.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Treprostinil sodium (SQ) (TREPROSTINIL SODIUM) Injection, 5.0 mg/ml; Regimen #1	UNK [0.00975 mg/ml], continuing; Subcutaneous use	Drug use for unknown indication (Product used for unknown indication)	Unknown; Unknown
#1) Treprostinil sodium (SQ) (TREPROSTINIL SODIUM) Injection, 5.0 mg/ml; Regimen #2	UNK, continuing; Subcutaneous use	Drug use for unknown indication (Product used for unknown indication)	24-SEP-2024 / 13-JUL-2025; 9 months 20 days

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2017 to Ongoing	Current Condition diagnosed 8 years ago	Pulmonary arterial hypertension (Pulmonary arterial hypertension);
Unknown	Historical Condition	Allergic rhinitis (Rhinitis allergic);

25b. Name And Address of Reporters continued
COSTA RICA

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: UNT-2025-024465

ADDITIONAL INFORMATION

NAME AND ADDRESS WITHHELD.

Ferrer

COSTA RICA