SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	COSTA RICA		PRIVACY		97 Years	Female	48.00 kg			2023

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

Diagnostic of hypertension [Hypertension]
Thinness [Skin thinness]

Case Description: This solicited case was received from a Consumer and concerned a patient participating in the patient support program (IC4-16257-001-CRI) in COSTA RICA.

The patient was a 97-year-old female (Weight: 48 kgs, Height: 160 cm) with medical history of Pacemaker and Heart rate problems since an unknown date in 2017.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ 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) IVABRADINE 5MG-F-42 (IVABRADINE) Film-coated tablet, 5 mg
#2) CARIVALAN 6.25mg/5mg (IVABRADINE 5 mg, CARVEDILOL 6.25 mg) **(Continued on Additional Information Page)**

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 10 mg, qd	#1) Oral use
#2) UNK	#2) Oral use

17. INDICATION(S) FOR USE
#1) Regulate heart rate problems (Heart rate abnormal)
#2) (Product used for unknown indication)

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 2017 / Unknown	#1) Unknown
#2) Unknown / MAY-2025	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) Xarelto (Rivaroxaban) ; 2017 / Ongoing

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	Procedure	
2017 to Ongoing	Historical Condition	Heart rate abnormal (Heart rate abnormal)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Servier PANAMA
COSTA RICA

26. REMARKS
Patient ID: 300940767
Study ID: IC4-16257-001-CRI*

24b. MFR CONTROL NO.
S25010250

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
25-JUL-2025

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient has been treated with IVABRADINE 5MG-F-42 (10 mg daily, orally) since an unknown date in 2017 to unknown date and then (10 mg daily) from unknown date in MAY-2025 for heart rate problems and CARIVALAN 6.25mg/5mg (unknown daily dose) since unknown date to unknown date in MAY-2025 used for unknown indication.

Other concomitant treatments included: Rivaroxaban (15 mg daily, orally) as a anticoagulant since an unknown date in 2017.

Since 2023, patient was diagnosed with hypertension. The intensity of the event and if it was related to the consumption of PROCOLARAN or CARIVALAN were not obtained.

Since unknown date, patient experienced Thinness, intensity of the event and if it was related to the consumption of PROCOLARAN or CARIVALAN were not obtained.

Treatment of the reaction (Diagnostic of hypertension): Since 2023 patient took Diovan 80 mg, 1 tablet daily, orally.

Action taken regarding IVABRADINE 5MG-F-42 and CARIVALAN 6.25mg/5mg: Drug withdrawn
Outcome: Not recovered for Diagnostic of hypertension and thinness.

The reporter’s assessed the case as non-serious.

The reporter’s causality assessment was not provided.

Consent to contact the doctor was not obtained.

Case Comment: Hypertension is listed in the RSI of IVABRADINE 5MG-F-42 and CARIVALAN 6.25mg/5mg, while skin atrophy is unlisted for both drugs. Given the reasonable chronology, age of patient, medical history and absence of recovery during drug continuation (IVABRADINE 5MG-F-42), the causal role of both drugs is assessed as possible.

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) IVABRADINE 5MG-F-42 (IVABRADINE) Film-coated tablet, 5 mg; Regimen #2	10 mg, qd; Oral use	Regulate heart rate problems (Heart rate abnormal)	MAY-2025 / Ongoing; Unknown
#2) CARIVALAN 6.25mg/5mg (IVABRADINE 5 mg, CARVEDILOL 6.25 mg) Tablet, 5/6.25 mg; Regimen #1	UNK; Oral use	(Product used for unknown indication)	Unknown / MAY-2025; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2017 to Ongoing	Procedure	Artificial cardiac pacemaker user (Cardiac assistance device user);