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			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
PRIVACY	GUATEMALA		PRIVACY		61 Years	Female	48.00 kg	30	JAN	2025	☐ PATIENT DIED ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING ☐ CONGENITAL ANOMALY ☒ OTHER

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
Gastrointestinal bleeding [Gastrointestinal bleeding]
Hemoglobin low [Hemoglobin low]
Diagnostic of Anemia [Anemia]
Diagnostic of glaucoma [Glaucoma]

Case Description: This solicited case was received from a Consumer in the GUATEMALA and concerned a patient participating in the post-authorization study (IC4-16257-001-GTM) (Improve adherence to treatments).

(Continued on Additional Information Page)

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) IVABRADINE 5MG-F-42 (IVABRADINE) Film-coated tablet, 5 mg
#2) Warfarina (Warfarina)
(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) Unknown

17. INDICATION(S) FOR USE
#1) Heart rate (Heart rate)
#2) Aortic valve and Coronary bypass (Aortic bypass)
(Continued on Additional Information Page)

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 2021 / FEB-2025	#1) Unknown
#2) 2021 / Ongoing	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) Rosuvastatina (Rosuvastatina) ; Ongoing
#2) Jardianz duo (Empagliflozin, Metformin hydrochloride) ; Ongoing

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

From/To Dates	Type of History / Notes	Description
2021 to Ongoing	Historical Condition	Heart rate (Heart rate)
2021 to Unknown	Historical Condition	Aortic valve replacement (Aortic valve replacement)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
SERVIER CENTRO AMERICA Y CARIBE
PANAMA

26. REMARKS
Patient ID: 2508932822201
Study ID: IC4-16257-001-GTM*

24b. MFR CONTROL NO.
S25008627

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

24c. DATE RECEIVED BY MANUFACTURER
17-JUN-2025

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

DATE OF THIS REPORT
24-JUN-2025

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was a 61-year-old female (Height: 155 cm and weight: 48 kg), with medical history of Heart rate since unknown date in 2021, treated with IVABRADINE 5MG-F-42 (10 mg daily) since unknown date in 2021 to since unknown date in FEB-2025, Aortic valve and Coronary bypass since unknown date in 2021, treated with WARFARINA (Unknown daily dose) since unknown date in 2021 and therapy was ongoing, Blood vessels problems since unknown date in 2021, treated with Rosuvastatina (20 mg daily, orally) since unknown date, Diabetes since unknown date in 2015, treated with Empagliflozin, Metformin hydrochloride (25 mg daily, orally) since unknown date and therapy was ongoing.

Co-suspect treatment included ACETYLSALICYLIC ACID (Unknown daily dose, orally) since unknown date in 2021 to unknown date in APR-2025 used for unknown indication.

Other medical history included Aortic valve replacement operation since unknown date in 2021.

No other concomitant treatment was reported if any.

On 30-Jan-2025, the patient experienced Gastrointestinal bleeding and for this her hemoglobin level dropped. Doctor told her that this happened because patient was taking two anticoagulants (WARFARINA And ASPIRINA) that they gave her at UNICAR since she had surgery in 2021. She was hospitalized from 30-Jan-2025 to 11-Feb-2025.

On 30-Jan-2025, she was diagnosed with anemia. Doctor told her that this happened because she was taking two anticoagulants (WARFARINA And ASPIRINA) that they gave her at UNICAR since she had surgery in 2021. In unknown date, while taking IVABRADINE 5MG-F-42, patient was diagnosed with Glaucoma because she had diabetes. No information was obtained on the Intensity of the event, if she related it to IVABRADINE 5MG-F-42 or whether the patient recovered.

Action taken regarding IVABRADINE 5MG-F-42: In Feb-2025, drug was discontinued, Doctor changed to PROCOLARAN 7.5MG.

Outcome: Recovering from Gastrointestinal bleeding, Low hemoglobin, Diagnostic of anemia, Unknown for Diagnostic of Glaucoma.

Consent to contact the doctor was obtained.

The reporter causality assessment for events (Gastrointestinal bleeding, low hemoglobin, diagnostic of anemia and diagnostic of glaucoma) was not related.

The reporter seriousness assessment was serious (Hospitalization) for events (Gastrointestinal bleeding, low hemoglobin, diagnostic of anemia) and serious (Medically significant) for event diagnostic of glaucoma.

Case Comment: Gastrointestinal hemorrhage, anemia, hemoglobin decreased and glaucoma are unlisted in the RSI of IVABRADINE 5MG-F-42. Given the use of both warfarin and aspirin, along with improvement despite drug continuation and events linked to increased bleeding risk, the causal role is assessed as unlikely for gastrointestinal hemorrhage, anemia and hemoglobin decreased. Due to reasonable chronology, but history of longstanding diabetes and missing information (outcome), the causal role for glaucoma 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
#2) Warfarina (Warfarina) ; Regimen #1	UNK; Unknown	Aortic valve and Coronary bypass (Aortic bypass) Aortic valve and Coronary bypass (Coronary artery bypass)	2021 / Ongoing; Unknown
#3) Aspirina (Acetylsalicylic acid) ; Regimen #1	UNK; Oral use	(Product used for unknown indication)	2021 / Ongoing; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2021 to Unknown	Historical Condition	Coronary bypass (Coronary artery bypass);
2021 to Ongoing	Historical Condition	Vascular disorder (Angiopathy);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2015 to Ongoing	Historical Condition	Diabetes (Diabetes mellitus);
Unknown to Ongoing	Historical Condition	Aortocoronary bypass (Coronary artery bypass);