# 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 |
| PRIVACY | COSTA RICA | | PRIVACY | | 26 Years | Female | 98.00 kg | | APR | 2025 |

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

Fading [Adverse event NOS]
Very low blood pressure [Blood pressure low]
Dizziness [Dizziness]
Nausea [Nausea]

Case Description: This solicited case was received from a Consumer in COSTA RICA and concerned a patient participating in the post-authorization study IC4-16257-001-CRI (patient ID: 116870271) (Improve adherence to treatments).

**(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 ) Digoxina (Digoxina)
**(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 ) 10 drops from Mo (Continued on Additional Information Page) | #2 ) Oral use |

17. INDICATION(S) FOR USE
#1 ) Chronotropsim (Heart rate abnormal)
#2 ) Chronotropism (Heart rate abnormal)

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

| 18. THERAPY DATES(from/to) | 19. THERAPY DURATION |
|---|---|
| #1 ) MAR-2025 / APR-2025 | #1 ) Unknown |
| #2 ) APR-2025 / APR-2025 | #2 ) Unknown |

## III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1 ) Bisoprolol (Bisoprolol) ; 02-JUN-2025 / Ongoing

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

| From/To Dates | Type of History / Notes | Description |
|---|---|---|
| 2006 to Ongoing | Historical Condition | Spina bifida (Spina bifida) |
| 2022 to Ongoing | Historical Condition | Single functional kidney (Single functional kidney) |
| | Single-kidney patient | |

## IV. MANUFACTURER INFORMATION

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

26. REMARKS
Patient ID: 116870271
Study ID: IC4-16257-001-CRI*

24b. MFR CONTROL NO.
**S25007757**

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

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

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

DATE OF THIS REPORT
10-JUN-2025

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

## ADDITIONAL INFORMATION

**7+13. DESCRIBE REACTION(S) continued**

The patient was a 26-year-old female (Height: 148 cm and weight: 98 kg) with a medical history of Chronotropism since an unknown date (diagnosed in APR-2025, patient already had the condition before the Servier medication), was treated with IVABRADINE 5MG-F-42 (10 mg daily, orally) from an unknown date in MAR-2025 to unknown date in APR-2025 and then since unknown date in APR-2025, DIGOXINA (10 drops from Monday to Friday, orally) from unknown date in APR-2025 to unknown date in APR-2025 and Bisoprolol (5 mg daily, orally) since 02-JUN-2025, Spina bifida since 2006, Single-kidney patient since 2022, Cardiorespiratory arrest since 2022 and Pituitary gland surgery for a brain tumor since 2022.

No other concomitant treatment was reported, if any.

On an unknown date in APR-2025, the patient experienced Fading, very low blood pressure, Dizziness and nausea due to DIGOXINA, so her doctor told her to return to IVABRADINE NOS. This happened 1 week after starting DIGOXINA and less than 1 month after stopping IVABRADINE 5MG-F-42.

On an unknown date, one week after discontinuing DIGOXINA the patient recovered from the adverse events.

Action taken with IVABRADINE 5MG-F-42: Not applicable

Action taken with DIGOXINA: Drug withdrawn

Outcome: Recovered.

The reporter causality for all events was reported as Not related with IVABRADINE 5MG-F-42.

Events were reported as non-serious.

Case Comment: Hypotension, dizziness and nausea are listed, while adverse event is unlisted as per IVABRADINE RSI. Taking into account the timing of events (with adverse events occurring one week after starting Digoxin and within one month after discontinuing IVABRADINE), the recovery observed upon restarting IVABRADINE as per the treating physician's recommendations, and the confounding factor of underlying conditions (chronotropism), the reporter's opinion was maintained, and the causal causal is assessed as not related.

**14-19. SUSPECT DRUG(S) continued**

| 14. SUSPECT DRUG(S) (include generic name) | 15. DAILY DOSE(S);<br>16. ROUTE(S) OF ADMIN | 17. INDICATION(S) FOR USE | 18. THERAPY DATES (from/to);<br>19. THERAPY DURATION |
|---|---|---|---|
| #1 ) IVABRADINE 5MG-F-42 (IVABRADINE) Film-coated tablet, 5 mg; Regimen #2 | 10 mg, qd (restarted); Oral use | Chronotropsim (Heart rate abnormal) | APR-2025 / Ongoing; Unknown |
| #2 ) Digoxina (Digoxina) ; Regimen #1 | 10 drops from Monday to Friday, orally; Oral use | Chronotropism (Heart rate abnormal) | APR-2025 / APR-2025; Unknown |

**23. OTHER RELEVANT HISTORY continued**

| From/To Dates | Type of History / Notes | Description |
|---|---|---|
| 2022 to Unknown | Historical Condition | Cardio-respiratory arrest (Cardio-respiratory arrest); |
| 2022 to Unknown | Historical Condition | Brain tumor operation (Brain tumour operation); |
| APR-2025 to Ongoing | Historical Condition | Heart rate abnormal (Heart rate abnormal); |