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	COSTA RICA		PRIVACY		45 Years	Female	Unk	12	MAR	2025	

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

Constipation [Constipation]
Stomach discomfort [Abdominal discomfort]
stomach pain [Abdominal pain upper]
anal irritation [Anorectal discomfort]
pain in the anal area [Proctalgia]
anal bleeding on occasion [Anal haemorrhage]
Physician prescribed Verzenio 150 mg once daily and 150 mg every 48 hours [Off label use]
Diarrhea on some occasions [Diarrhoea]

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Abemaciclib (Abemaciclib) Tablet
#2) LOPERAMIDE (LOPERAMIDE) Unknown
(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) 150 mg, bid	#1) Oral
#2) UNK, other (eve (Continued on Additional Information Page)	#2) Unknown

17. INDICATION(S) FOR USE
#1) Breast cancer (Breast cancer)
#2) Diarrhea (Diarrhoea)

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 03-MAR-2023 / Unknown	#1) Unknown
#2) Unknown	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) EXEMESTANE (EXEMESTANE) Unknown ; Unknown
#2) VITAMIN D [VITAMIN D NOS] (VITAMIN D [VITAMIN D NOS]) Unknown ; Unknown
#3) CALCIUM (CALCIUM) Unknown ; Unknown
#4) ENALAPRIL (ENALAPRIL) Unknown ; Unknown
#5) OMEPRAZOLE (OMEPRAZOLE) Unknown ; Unknown

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

From/To Dates	Type of History / Notes	Description
Unknown	Medical Condition	Arterial hypertension (Hypertension)
		The pressure only increases when she goes to the doctor, according to the patient.
Unknown	Procedure	Chemotherapy (Chemotherapy)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Eli Lilly Interamerica Inc (AR Branch)
Tronador 4890 - Piso 12
Buenos Aires, Capital Federal CP: 1430 ARGENTINA
Phone: 54 1145464000

26. REMARKS

24b. MFR CONTROL NO.
CR202503014682

24c. DATE RECEIVED BY MANUFACTURER
30-MAY-2025

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

DATE OF THIS REPORT
05-JUN-2025

25a. REPORT TYPE
☐ INITIAL ☒ FOLLOWUP: 2

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

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Case Description: This solicited case, reported by a consumer via a patient support program (PSP) from a business partner, with additional information from the initial reporter via PSP from a business partner, concerned a 45-year-old female patient of unknown ethnicity.

Medical history included high blood pressure, chemotherapy and radiation therapy. Concomitant medications included vitamin D and calcium for unknown indications, enalapril for blood pressure, and omeprazole for prevention of gastric discomfort.

The patient received abemaciclib (Verzenio) tablets, 150 mg, twice daily, via oral, for the treatment of breast cancer, beginning on 03-Mar-2023 or 23-Mar-2023 (conflicting information provided by reporter). As concomitant chemotherapy she received exemestane for breast cancer. On an unknown date, abemaciclib therapy was suspended due to unknown circumstances, and restarted on an unknown date, at an unknown dose and frequency. Since an unknown date, she received loperamide (unknown manufacturer), each time she took abemaciclib, to prevent diarrhea which started on 12-Mar-2025. Dose, formulation, route of administration and start date were not provided. On 12-Mar-2025, after starting loperamide therapy, she experienced constipation and on same day, as per her treating physician instruction, she started to follow the dosage regimen of abemaciclib as 150 mg every 48 hours for one week (every other day), then increased to150 mg every 24 hours for second week (off label use) and 150 mg every 12 hours for third week. On an unknown date in Mar-2025, she experienced stomach pain; and when she went to the bathroom experienced pain in the anal area with bleeding on occasions that her doctor indicated was irritation from the constipation she initially had. When she started taking abemaciclib at a dose of 150 mg every 12 hours during the third week, she no longer experienced constipation. However, she had been experiencing stomach discomfort during the day and diarrhea on some occasions. There were days when she had gone to the bathroom six times, with stools a little softer than normal. She had a hard time making dietary changes, but the changes started to help reduce the effects of diarrhea. On an unknown date, diarrhea made anal irritation worse, but the doctor did not prescribe any medication, only indicated to continue the diet without irritants. No treatment was given for constipation. On 12-Apr-2025, diarrhea and constipation got resolved. Since 15-Apr-2025, her stomach pain and stomach discomfort was improving; she felt better for a week and was defecating three to four times a day with a softer consistency and had less stomach pain. The outcome of off label use and anal irritation was unknown, while outcome for the remaining events was recovering. Information regarding further corrective treatments and loperamide status was not provided. Abemaciclib therapy was ongoing. Follow-up was not possible as the reporter refused to be contacted further or to contact their treating physician.

The reporting consumer related constipation and diarrhea while did not provide relatedness of the rest of events with abemaciclib therapy but related the event of constipation to loperamide therapy, and did not provide an opinion of relatedness between remaining events and loperamide treatment.

Update 19-Mar-2025: This case was determined to be non-valid as there was no identifiable valid adverse event. The report described the event of off label use.

Update 21-Mar-2025: Initially this case was considered as non-valid as no adverse event was reported. Additional information was received from initial reporter via PSP on 18-Mar-2025, including a valid adverse event. Added one non-serious event of constipation. Also added loperamide as suspect drug, abemaciclib lot number and expiration date, exemestane, vitamin D, calcium, enalapril and omeprazole as concomitant drugs, high blood pressure, chemotherapy and radiotherapy as relevant history. Updated abemaciclib therapy status to ongoing and narrative accordingly.

Update 24-Mar-2025: Additional information was received from initial reporter via PSP on 20-Mar-2025 regarding correction in the information received on 18-Mar-2025. Updated abemaciclib therapy restart date from 16-Feb-2025 to unknown, and narrative accordingly.

Update 14-Apr-2025: Additional information was received from the initial reporter via PSP on 09-Apr-2025. Added two non-serious events of stomach discomfort and diarrhea. Updated outcome of event for constipation from not recovered to recovered. Updated the narrative accordingly.

Update 29-Apr-2025: Additional information was received on 22-Apr-2025 from the reporting consumer via PSP of a business partner. Added non-serious events of abdominal pain upper, proctalgia, anal hemorrhage and anorectal discomfort. Updated outcome of diarrhea and abdominal discomfort, both to recovering. Upon internal review of previous information, it was updated start date and frequency of initial dosage regimen of abemaciclib, and loperamide status. Narrative was updated accordingly with new information.

Update 04-Jun-2025: Additional information was received on 30-May-2025 from the reporting consumer via PSP of a business partner. Added start date, stop date of event constipation and diarrhea. Treatment received as no for event constipation. Updated causality of event constipation, diarrhea to yes and narrative accordingly with new information.

Lilly Analysis Statement: 04-Jun-2025: The company considered the unlisted event of constipation unrelated to the Verzenio (abemaciclib).

Mfr. Control Number: CR202503014682

ADDITIONAL INFORMATION

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) Abemaciclib (Abemaciclib) Tablet; Regimen #2	UNK UNK, unknown; Oral	Breast cancer (Breast cancer)	Unknown; Unknown
#1) Abemaciclib (Abemaciclib) Tablet; Regimen #3	150 mg, other (every 48 hours); Oral	Breast cancer (Breast cancer)	12-MAR-2025 / Unknown; Unknown
#1) Abemaciclib (Abemaciclib) Tablet; Regimen #4	150 mg, daily (every 24 hours); Oral	Breast cancer (Breast cancer)	Unknown; Unknown
#1) Abemaciclib (Abemaciclib) Tablet {Lot # D761191; Exp.Dt. OCT-2026}; Regimen #5	150 mg, bid (every 12 hours); Oral	Breast cancer (Breast cancer)	Ongoing; Unknown
#2) LOPERAMIDE (LOPERAMIDE) Unknown; Regimen #1	UNK, other (everytime she takes abemaciclib); Unknown	Diarrhea (Diarrhoea)	Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Procedure	Radiation therapy (Radiotherapy);