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		53 Years	Female	Unk	27	MAR	2024	

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

Dehydration [Dehydration]
A lot of stomach pain [Abdominal pain upper]
felt very down/ Decay [Depressed mood]
A lot of insomnia [Insomnia]
Dry cough [Cough]
reflux [Gastrooesophageal reflux disease]
Mood swings/sensitive in her emotions/bit irritable [Mood swings]
Bone pain [Bone pain]
severe pain that has been increasing in the area of the mastectomy surgery [Procedural pain]

(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 {Lot # D669613; Exp.Dt. APR-2026}
#2) LOPERAMIDE (LOPERAMIDE) Unknown, 2 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) 150 mg, bid	#1) Oral
#2) 2 mg, unknown	#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) 27-MAR-2024 / 23-MAY-2024	#1) 1 month 27 days
#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) ANASTROZOLE (ANASTROZOLE) Unknown ; Unknown
#2) ARIMIDEX (ANASTROZOLE) Unknown, 1 mg; DEC-2023 / Unknown
#3) CALCIUM (CALCIUM) Unknown, 600 mg; Unknown
#4) VITAMIN D [COLECALCIFEROL] (COLECALCIFEROL) Unknown ; Unknown
#5) VITAMIN B NOS (VITAMIN B NOS) Unknown ; Unknown
#6) ZOMETA (ZOLEDRONIC ACID MONOHYDRATE) Injection ; 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	Irritable bowel syndrome (Irritable bowel syndrome)
Unknown	Medical Condition	Constipation (Constipation)

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.

CR202404006881

24c. DATE RECEIVED BY MANUFACTURER

25-MAR-2025

24d. REPORT SOURCE

☒ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT

28-MAR-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

the pain increased to the point where the patient can no longer move the right arm [Mobility decreased]
Diarrhea/ had moderate diarrhea [Diarrhoea]
Nausea [Nausea]
Very tired [Fatigue]
taste of coffee was more bitter [Dysgeusia]

Case Description: This solicited case, reported by a consumer via a patient support program (PSP) through a business partner, concerned a 53-years-old female patient of unknown origin.

Medical history included diabetes, constipation, irritable bowel syndrome, and a bone densitometry test, which diagnosed osteopenia in 2020, approximately four years before the cancer diagnosis. She underwent chemotherapy from 27-Jul-2023 to 08-Nov-2023, receiving a total of eight sessions (four red and four white). An ear specialist suggested that chemotherapy possibly caused her hearing loss, which began in early March 2024. She also received radiotherapy from 28-Feb-2024 to 19-Mar-2024, totaling 15 sessions, for breast cancer. Concomitant medications included calcium and vitamin B for osteopenia, and zoledronic acid monohydrate, vitamin D, and electrolytes orally for unknown indications.

The patient received abemaciclib (Verzenio) tablets of 150 mg, 300 mg daily (one tablet in the morning and one in the evening), orally, for the treatment of breast cancer, beginning on 27-Mar-2024 or 09-Apr-2024 (conflicting date). Concomitant chemotherapy included anastrozole. Since 27-Mar-2024, she experienced diarrhea during the first three days of treatment, along with feeling very tired, with too much nausea and a lot of insomnia. She did not take any medication for nausea as it was not frequent. On an unknown date, after taking abemaciclib therapy, she experienced a lot of stomach pain. When she had two or three episodes of diarrhea and it was constant, as corrective treatment she took loperamide, 2mg, but when diarrhea only occurred once she did not take loperamide because sometimes the discomfort went away. As corrective treatment for stomach pain, she took omeprazole, which had relieved her a lot. On an unknown date, nausea and tiredness went away, but the stomach pain and diarrhea persisted. Regarding insomnia, she had problems probably due to the stomach pain she had those days, the insomnia affected her more. Regarding tiredness, it was unknown if it was a reaction to the radiotherapy because she had already finished it. In general, she felt a little recovered from the symptoms, but not 100%. On an unknown date in Apr-2024, her diarrhea was less, on 08-Apr-2024 she did not have diarrhea and on 09-Apr-2024 she did not have diarrhea either. Currently when she drank coffee, she felt reflux, and the taste of coffee was more bitter. She consumed little milk but since she had been taking the therapy she had noticed that she got stomach pain (regardless of what she ate) and when she drank milk the pain was stronger. On 25-Apr-2024, she experienced moderate diarrhea six times a day and felt very low. She referred that with loperamide she got very strong stomach pains. She was advised to stop the medication for a week and to restart it on 03-May-2024. On 23-May-2024, her physician discontinued abemaciclib therapy due to her poor health from numerous side effects, including severe diarrhea, extreme tiredness, and insomnia. On an unknown date, she experienced mood swings as emotional sensitivity, and bit irritability. She used loperamide treat diarrhea. She also used bifidobacterium breve, bifidobacterium infantis, lactobacillus acidophilus, lactobacillus bulgaricus, lactobacillus casei, lactobacillus rhamnosus, and streptococcus thermophilus (multiflora) tablet once daily for five days to treat diarrhea after discontinuing abemaciclib therapy. On an unknown date in Jul-2024, she restarted her abemaciclib dose and her dose was reduced to 200 mg per day as 300 mg per day dose was causing her extreme diarrhea, because in one single night in 2 hours she went 14 times to the bathroom, then she had to go to the emergency room because she was already totally dehydrated and there was no liquid to help her. After that she was hospitalized due to dehydration. She also suffers from a lot of bone pain and tiredness. On an unknown date, she had mastectomy surgery, during which 14 lymph nodes were removed (due to unspecified reason). On an unknown date, she had severe pain that has been increasing in the area of the mastectomy surgery, the pain increased to the point where the patient can no longer move the right arm. She used to take acetaminophen for bone pain and procedural pain. She took tramadol hydrochloride for procedural pain. After treatment, her pain was decreased. As of 12-Mar-2025, her pain was 6/10 (unit not provided). She had a very unusual, dry, bothersome cough that worsened at night. She has not had a cold, has not sought medical attention, or was not taking anything. Information regarding the corrective treatment and details regarding hospitalization was not provided. Outcomes for event of nausea, fatigue was resolved mood swings, outcome for events of bone pain, insomnia and diarrhea was resolving, outcome for events of mobility decreased and depression were unknown, and the other events had not resolved. Abemaciclib therapy was discontinued, and restarted at reduced dose. The status of loperamide was not provided.

The initial reporting consumer assessed insomnia and dehydration, did not know the relatedness for event mood swings and bone pain while did not provide relatedness assessment for the remaining events with abemaciclib therapy. The consumer related upper abdominal pain to loperamide therapy but did not provide a relatedness assessment for the remaining events.

Update 17-Apr-2024: Additional information was received from the initial reporter via PSP on 10-Apr-2024. Added three medical history, one concomitant drug, onset date of event diarrhea and two non-serious events of esophageal reflux and taste bitter. Updated narrative with new information.

Update 01-May-2024: Additional information was received from the initial reporter via PSP on 26-Apr-2024. Added severity of diarrhea, one non-serious event of depressed mood. Updated loperamide from treatment drug to co-suspect, event description of diarrhoea and narrative with new information.

Update 06-Jun-2024: Additional information received on 31-May-2024, by the initial reporting consumer via PSP (Processed together). Action take for abemaciclib therapy updated as drug discontinue. Added one treatment drug multiflora. Added one

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

non-serious event term mood swings. For the event insomnia updated outcome as recovering and relatedness as 'Yes'. Narrative updated with new information.

Update 13-Jun-2024: Additional information was received from the initial reporting consumer via business partner on 07-Jun-2024. Updated complete date of abemaciclib discontinuation and narrative with new information.

Update 26-Jul-24: Additional information was received from the initial reporter via PSP on 23-Jul-2024 and case was upgraded to serious. Added one serious event of dehydration, one non serious event of bone pain, updated outcome of insomnia to not recovered and narrative with new information.

Update 22-Aug-2024: Information was received from initial reporting consumer on 19-Aug-2024 via PSP. No new medically significant information was received. No changes were made to the case.

Update 08-Feb-2025: Additional information was received from the initial reporter via PSP on 04-Feb-2025. Added dose of co-suspect drug loperamide and one concomitant drug of omeprazole and two non serious events of post procedural pain and mobility decreased. Updated the outcome of the event diarrhea from not recovered to recovering and narrative with new information.

Update 17-Mar-2025: Additional information was received from the initial reporter via PSP through a business partner on 12-Mar-2025. Added one lab data of pain scale, start date in previously captured dosage regimen (D669346) of abemaciclib and one treatment drug of tramadol hydrochloride. Updated outcome of event post procedural pain from unknown to resolving, outcome of bone pain from not resolved to resolving, and narrative with new information.

Update 27-Mar-2025: Additional information was received from the initial reporter via PSP through a business partner on 23-Mar-2025. Added a non-serious event of cough. Updated narrative accordingly.

Update 28-Mar-2025: Additional information was received from the initial reporter via PSP through a business partner on 25-Mar-2025. Updated the seriousness criteria for the event of dehydration from medically significant to hospitalized and narrative with new information.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	12-MAR-2025	Pain assessment Unit not provided	6	10 0

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 {Lot # D669346; Exp.Dt. APR-2026}; Regimen #2	100 mg, bid; Oral	Breast cancer (Breast cancer)	JUL-2024 / Ongoing; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Medical Condition	Diabetes (Diabetes mellitus);
2020 to Unknown	Medical Condition	Osteopenia (Osteopenia);
MAR-2024 to Unknown	Historical AR Due to chemotherapy	Auditory disorder (Auditory disorder);
27-JUL-2023 to 08-NOV-2023	Procedure A total of 8 chemotherapies 4 red and 4 white.	Chemotherapy (Chemotherapy);
28-FEB-2024 to 19-MAR-2024	Procedure A total of 15	Radiotherapy (Radiotherapy);
Unknown	Procedure	Bone densitometry (Bone densitometry);