SUSPECT ADVERSE REACTION REPORT

PA-TOLMAR, INC.-24PA055075

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE Years	3. SEX	4-6 REACTION ONSET		
		Day	Month	Year			Day	Month	Year
LGG	PANAMA	18	May	1941	82	Male			2024

7+13 DESCRIBE REACTION(S) (including relevant tests/lab data)

1) Stroke/Cerebrovascular infarction, bedridden, has a tube to feed him (Cerebrovascular infarction (10060772), Cerebral infarction (10008118))
(/Nov/2024 - 21/Dec/2024) - Fatal
2) PATIENT IS CURRENTLY IN A BAD CONDITION (General physical health deterioration (10049438), General physical health deterioration (10049438))
(//2024 -) - Not Recovered/Not Resolved/Ongoing
3) NO LONGER SPEAKS (Speech loss (10041470), Aphasia (10002948))
(//2024 -) - Not Recovered/Not Resolved/Ongoing
4) THEY ARE ONLY WAITING FOR THE PATIENT TO DIE (Terminal state (10048669), Terminal state (10048669))
(//2024 -) - Not Recovered/Not Resolved/Ongoing

Cont..

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [x] PATIENT DIED
- [x] LIFE THREATENING
- [x] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] RESULTS IN PERSISTENCE OR SIGNIFICANT DISABILITY/INCAPACITY
- [ ] CONGENITAL ANOMALY
- [x] OTHER MEDICALLY IMPORTANT CONDITION

II. SUSPECT DRUG(S)INFORMATION

14. SUSPECT DRUG(S)(include generic name)

1) Eligard® (Leuprolide acetate) (Leuprolide acetate) (Suspect) (Injection)(Unknown)(Unknown)(Unknown)

Cont..

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☑ NA

15. DAILY DOSE(S)

1) (45 milligram(s), 1 in 6 Month)

2) (45 milligram(s), 1 in 6 Month)

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous
2) Subcutaneous

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ NA

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
(Oct-2024 -)	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

1)Abiraterone(ABIRATERONE)(Tablet)

Cont..

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

1) PROSTATE CANCER (10060862, Prostate cancer) (Continuing: Yes)

Cont..

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER

Name : Tolmar, Inc
701 Centre Avenue
Fort Collins, CO, 80526, UNITED STATES OF AMERICA
debbie.maierhofer@tolmar.comand+1-4129158447

Study Information
Study Name: NA
EudraCT Number:
Protocol No.: N/A
Center No.:
Subject Id :

24.REPORT NULLIFIED	24b. MFR CONTROL NO.
☐ YES ☐ NO	PA-TOLMAR, INC.-24PA055075
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
07/Apr/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
18/Apr/2025	☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) (Continuation...)

5) CANCER ADVANCED (METASTASIZED) AND BEGAN TO COMPROMISE HIS ORGANS (Prostate cancer metastatic (10036909), Prostate cancer metastatic (10036909)(//2024 -) - Not Recovered/Not Resolved/Ongoing)

6) the patient was in a coma (Coma (10010071), Coma (10010071)(/Nov/2024 -) - Unknown)

Event Description :

This Study report from PANAMA was received by Adium via Asofarma a tu lado Patient Support Program (reference number: PA-ADIUM-PA-0065-20241217) on 17-DEC-2024 from a Consumer/Other Non-Health Prof regarding an Elderly 83 Years old Male patient who experienced the important medical events of Patient is currently in a bad condition (General physical health deterioration), No longer speaks, (Speech loss), Cancer advanced (metastasized) and began to compromise his organs (Prostate cancer metastatic), Cerebrovascular infarction, cannot move, has a tube to feed him (Cerebrovascular infarction), They are only waiting for the patient to die (Termial state) during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 18-DEC-2024.

The patient's medical history and current conditions included Prostate cancer, Feeding tube insertion.

Concomitant medications were not reported.

On 24-MAR-2023, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration dates were not provided). On OCT-2024, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration dates were not provided). On an unknown date on NOV-2024 (reported as a month ago, approximately one month after the most recent dose of Eligard, he underwent tomography exams (contrasted TAC) to verify all the organs and, based on the results, was told that the cancer advanced (metastasized) and began to compromise his organs. On an unspecified date around DEC-2023 (reported as three weeks ago), the patient had a cerebrovascular infarction, for this reason, he was in a bad condition, bedridden, could not move, he no longer spoke and had a tube to feed him. They are only waiting for the patient to die. Corrective treatment was not reported.

Relevant test results included:
2024: Computerised tomogram: the cancer advanced (metastasized) (Ref range: Not provided)

Action taken with Eligard in response to the events was Unknown. De-challenge and re-challenge were Not applicable. The outcome of General physical health deterioration, Speech loss, Prostate cancer metastatic, Cerebrovascular infarction and Terminal state was Not Recovered/Not Resolved.

The reporter did not assess the seriousness or causality of the events in relationship to Eligard.

Information received from Tolmar business partner, who is responsible for follow-up, as per the SDEA.

Evaluator comment (Tolmar): This is regarding an elderly 83-year-old male patient who experienced cerebral infarction (Cerebrovascular infarction), prostate cancer metastatic (Cancer advanced - metastasized and began to compromise his organs), general physical health deterioration (Patient is currently in a bad condition) and is in terminal state (only waiting for the patient to die) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed all the events as serious (MS) as they are IME events and require significant medical intervention. Cerebral infarction is considered as related to Eligard (drug) based on the close temporal relationship and consistency of the event with product safety profile, while all other events are considered not related to Eligard (drug) as there is no reasonable evidence and alternative causal explanation is available. Events general physical health deterioration and terminal state are attributable to cerebral infarction based on the case context. Prostate cancer metastatic is due to underlying prostate cancer as progression is inherent to it despite treatment. Elderly age and underlying malignancy are strong confounders for all the events. All the events are not related to device component of Eligard.

On 07-Apr-2025, follow-up information was received by Adium (reference number: PA-ADIUM-PA-0065-20241217) via an email from the Patient Support Program from a consumer (husband of a patient's niece) (non-healthcare professional) and sent to Tolmar on 08-Apr-2025. New information included: Case level seriousness updated to Death, Life threating and Prolonged hospitalization. Patient's death details added. Event “Cerebral infarction” verbatim updated from "Cerebrovascular infarction, bedridden, has a tube to feed him" to "Stroke/Cerebrovascular infarction, bedridden, has a tube to feed him", stop date added, outcome updated from “not recovered” to “fatal”, seriousness added as Death, life threatening and prolonged hospitalization. New serious event added 'the patient was in a coma' (Coma) (prolonged hospitalization). Concomitant medication added as Abiraterone.

Concomitant medication included Abiraterone.

On an unknown date, the patient became ill and received the dose at home because the patient could not move. Additionally, the patient underwent with some tests and CAT scan at the hospital and based on results, a stroke was diagnosed. He took abiraterone for approximately 1 week and stopped taking it because he had a stroke.

On an unspecified date in Nov-2024, the patient had cerebrovascular infarction. It was noticed that patient was already hospitalized at the time the cerebrovascular infarction occurred. As a result, the patient was in a coma for one month and two weeks. The patient's family was subsequently informed that nothing further could be done for the patient, so the relatives took him home and treated him.

Continuation Sheet for CIOMS report

On 21-Dec-2024, the patient passed away due to sudden cerebrovascular infarction. The patient was 83 years old at the time of his death. It was unclear whether an autopsy was performed. No further details were available.

Relevant test results included:
On an unknown date: CAT scan (Computerised tomogram): a stroke was diagnosed.

Action taken with Eligard in response to the events was not applicable. De-challenge and re-challenge were not applicable.

On 21-Dec-2024, the outcome of cerebral infarction was fatal.

The outcome of coma was unknown.

The reporter assessed the seriousness of cerebral infarction (death, life threating and prolonged hospitalization) and coma (prolonged hospitalization) as serious.

The reporter did not provide the causality of cerebral infarction, coma in relationship to Eligard and Eligard Unspecified device.

No follow-up queries raised.

Listedness of the events general physical health deterioration, aphasia, terminal state, prostate cancer metastatic is retained as per previous assessment.

Coma>Eligard>Unlisted as per CCDS>07-Nov-2024
Coma>Eligard>Unlisted as per USPI>Feb-2025
Coma>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Coma>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Listedness Updated for Cerebral infarction
Cerebral infarction>Eligard>Unlisted as per CCDS>07-Nov-2024
Cerebral infarction>Eligard>Unlisted as per USPI>Feb-2025
Cerebral infarction>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Cerebral infarction>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding an elderly 83-year-old male patient who experienced cerebral infarction (Cerebrovascular infarction), prostate cancer metastatic (Cancer advanced - metastasized and began to compromise his organs), general physical health deterioration (Patient is currently in a bad condition) and is in terminal state (only waiting for the patient to die) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed all the events as serious (MS) as they are IME events and require significant medical intervention. Cerebral infarction is considered as related to Eligard (drug) based on the close temporal relationship and consistency of the event with product safety profile, while all other events are considered not related to Eligard (drug) as there is no reasonable evidence and alternative causal explanation is available. Events general physical health deterioration and terminal state are attributable to cerebral infarction based on the case context. Prostate cancer metastatic is due to underlying prostate cancer as progression is inherent to it despite treatment. Elderly age and underlying malignancy are strong confounders for all the events. All the events are not related to device component of Eligard.

Follow-up event added coma ('the patient was in a coma') during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed the events cerebral infarction as serious (Death, life threatening and prolonged hospitalization) and Coma (prolonged hospitalization). Event coma is attributable to cerebral infarction based on the case context. The event cerebral infarction is reassessed as not related to Eligard (Drug and device) considering the elderly age and underlying malignancy.
Causality of the events, general physical health deterioration, aphasia, terminal state, prostate cancer metastatic is retained as per previous assessment.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
CAT SCAN			
CONTRASTED TAC	//2024		

Test Result (Code) / Result Unstructured Data (free text) :

1) Test Name: CAT SCAN

Continuation Sheet for CIOMS report

Result Unstructured Data (free text) : a stroke was diagnosed
Test Date:

2) Test Name: CONTRASTED TAC

Result Unstructured Data (free text) : Cancer advanced (metastasized)
Test Date: //2024
Lab Comments :

2) Test Name : CONTRASTED TAC
Lab Comments : Cancer advanced (metastasized)

14.SUSPECT DRUG(S) (Continuation...)

Product-Reaction Level

1) Drug	:	Eligard® (Leuprolide acetate)
Active Substance	:	1) Leuprolide acetate
Drug Characterization	:	Suspect
Form of Admin	:	1) Injection
		2) Injection
		3) Injection
Lot Number	:	1) Unknown
		2) Unknown
		3) Unknown
Daily Dose	:	(45 milligram(s), 1 in 6 Month)
		(45 milligram(s), 1 in 6 Month)
		(45 milligram(s), 1 in 6 Month)
Route of Admin	:	1) Subcutaneous
		2) Subcutaneous
		3) Subcutaneous
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	2) From : /Sep/2022 To :Not applicable
		3) From : 24/Mar/2023 To :Not applicable
Action(s) Taken With Drug	:	Not applicable

Causality

1) Stroke/Cerebrovascular infarction, bedridden, has a tube to feed him (Cerebrovascular infarction - 10060772, Cerebral infarction - 10008118)

Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

2) PATIENT IS CURRENTLY IN A BAD CONDITION (General physical health deterioration - 10049438, General physical health deterioration - 10049438)

Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

3) NO LONGER SPEAKS (Speech loss - 10041470, Aphasia - 10002948)

Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

4) THEY ARE ONLY WAITING FOR THE PATIENT TO DIE (Terminal state - 10048669, Terminal state - 10048669)

Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

5) CANCER ADVANCED (METASTASIZED) AND BEGAN TO COMPROMISE HIS ORGANS (Prostate cancer metastatic - 10036909, Prostate cancer metastatic - 10036909)

Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

6) the patient was in a coma (Coma - 10010071, Coma - 10010071)

Causality as per reporter	:	Not Reported

Continuation Sheet for CIOMS report

Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Stroke/Cerebrovascular infarction, bedridden, has a tube to feed him
CORE UnLabeled
2) PATIENT IS CURRENTLY IN A BAD CONDITION
CORE UnLabeled
3) NO LONGER SPEAKS
CORE UnLabeled
4) THEY ARE ONLY WAITING FOR THE PATIENT TO DIE
CORE UnLabeled
5) CANCER ADVANCED (METASTASIZED) AND BEGAN TO COMPROMISE HIS ORGANS
CORE Labeled
6) the patient was in a coma
CORE UnLabeled

2) Drug : Eligard® Unspecified Device (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form of Admin : 1) Injection
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

1) Stroke/Cerebrovascular infarction, bedridden, has a tube to feed him (Cerebrovascular infarction - 10060772, Cerebral infarction - 10008118)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
2) PATIENT IS CURRENTLY IN A BAD CONDITION (General physical health deterioration - 10049438, General physical health deterioration - 10049438)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
3) NO LONGER SPEAKS (Speech loss - 10041470, Aphasia - 10002948)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
4) THEY ARE ONLY WAITING FOR THE PATIENT TO DIE (Terminal state - 10048669, Terminal state - 10048669)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
5) CANCER ADVANCED (METASTASIZED) AND BEGAN TO COMPROMISE HIS ORGANS (Prostate cancer metastatic - 10036909, Prostate cancer metastatic - 10036909)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
6) the patient was in a coma (Coma - 10010071, Coma - 10010071)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related

Labeling :

1) Stroke/Cerebrovascular infarction, bedridden, has a tube to feed him
CORE
2) PATIENT IS CURRENTLY IN A BAD CONDITION
CORE
3) NO LONGER SPEAKS
CORE
4) THEY ARE ONLY WAITING FOR THE PATIENT TO DIE
CORE
5) CANCER ADVANCED (METASTASIZED) AND BEGAN TO COMPROMISE HIS ORGANS
CORE
6) the patient was in a coma
CORE

15. DAILY DOSE(S) (Continuation...)

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

Continuation Sheet for CIOMS report

2) 45 milligram, q 6 month

3) 45 milligram, q 6 month

Drug 2 :Eligard® Unspecified Device

1) UNK

22.CONCOMITANT DRUG(S) (Continuation...)

1). Drug	:	Abiraterone
Active Substance	:	1) ABIRATERONE
Form Strength	:	
Form of Admin	:	1) Tablet
Daily Dose	:	1) (250 milligram(s), in 1 Day)
Indications	:	1) prostate cancer [10060862 - Prostate cancer]
Dosage Text	:	1) 4 tablets daily for 1 month (120 pills)

23. OTHER RELEVANT HISTORY (Continuation...)

2) FEEDING TUBE INSERTION (10051041 , Feeding tube insertion)