

SUSPECT ADVERSE REACTION REPORT PA-Tolmar-TLM-2025-01013												

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE Years	3. SEX	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
W-P	PANAMA	Day	Month	Year	81	Male	Day	Month	Year	
		08	Apr	1944			09	Apr	2025	
7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) 1) Hospitalized for multiple cerebral ischemias (Cerebral ischemia (10008121), Cerebral ischaemia (10008120)) (09/Apr/2025 -) - Unknown 2) Completely decompensated (Chronic disease (10076311), Chronic disease (10076311)) (15/Apr/2025 -) - Not Recovered/Not Resolved/Ongoing 3) Completely decompensated (Condition worsened (10076326), Condition aggravated (10010264)) (15/Apr/2025 -) - Not Recovered/Not Resolved/Ongoing 4) Fever (Fever (10016558), Pyrexia (10037660)) (12/May/2025 -) - Unknown										☐ PATIENT DIED ☒ LIFE THREATENING ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION ☒ RESULTS IN PERSISTENCE OR SIGNIFICANT DISABILITY/INCAPACITY ☐ CONGENITAL ANOMALY ☒ 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)		Cont..	20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA 21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☒ NA (NA : Not Applicable)
15. DAILY DOSE(S) 1) (45 milligram(s), 1 in 6 Month)	Cont..	Cont..	
16. ROUTE(S) OF ADMINISTRATION 1) Subcutaneous		Cont..	
17. INDICATION(S) FOR USE 1) Prostate cancer [10060862 - Prostate cancer]		Cont..	
18. THERAPY DATE(S) (from/to) 1) (01/Apr/2024 - ongoing)		19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction) No concomitants used/reported	
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) 1) PROSTATE CANCER (10060862, Prostate cancer) (Continuing: Yes)	

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.: NA Center No.: Subject Id :	
24. REPORT NULLIFIED ☐ YES ☐ NO	24b. MFR CONTROL NO. PA-Tolmar-TLM-2025-01013		
24c. DATE RECEIVED BY MANUFACTURER 12/May/2025	24d. REPORT SOURCE ☒ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL		
DATE OF THIS REPORT 23/May/2025	25a. REPORT TYPE ☐ INITIAL ☒ FOLLOWUP		

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) High blood sugar/ Sugar 225 (Blood glucose increased (10005557), Blood glucose increased (10005557)(15/Apr/2025 -) - Not Recovered/Not Resolved/Ongoing)

6) Fainting after ingestion of Xtandi (Fainting (10016169), Syncope (10042772)(12/May/2025 -) - Unknown)

7) Blood pressure 64/34 (Blood pressure low (10005753), Hypotension (10021097)(12/May/2025 -) - Unknown)

8) due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May 2025, (Intentional dose omission (10079221), Intentional dose omission (10079221)(/May/2025 -) - Unknown)

Event Description :

This Invalid case report from PANAMA was received by Adium PSP - Prevenfuturo (reference number: PA-ADIUM-PA-0023-20250317) on 17-MAR-2025 from Consumer/Other Non-Health Prof and sent to Tolmar on 18-MAR-2025.

This report was assessed as invalid as no adverse event was reported. The reported term was not considered an adverse event because the reason for the surgery was not provided.

Abbreviated Narrative

This report was assessed as invalid as no adverse event was reported. The reported term was not considered an adverse event because the reason for the surgery was not provided. This report was assessed as invalid as no adverse event was reported. The reported term was not considered an adverse event because the reason for the surgery was not provided.

On 21-Apr-2025, follow up information was received by Adium (reference number: PA-ADIUM-PA-0023-20250317) from a consumer (family member) and sent to Tolmar on 22-Apr-2025. New information included: Case upgraded from invalid to valid. New serious (hospitalization and medically significant) events added as "High blood sugar" (Blood glucose increased) and 'Completely decompensated' (Chronic disease and condition aggravated). Lab investigation added as "blood glucose". Action taken updated.

The patient's medical history was unknown and current condition included prostate cancer.

Concomitant medications were Xtandi (enzalutamide).

On 13-Mar-2025, the patient had a toe to be amputated.

On Tuesday, 18-Mar-2024, the discharge from the hospital was anticipated. No further details were provided.

On 01-Apr-2024, the patient began receiving Eligard 45 mg every 6 months via subcutaneous route for prostate cancer (Lot numbers and expiration dates were unknown).

On 15-Apr-2025, the patient had been hospitalized due to elevated blood sugar level and was found to be completely decompensated. No further details were provided.

Corrective treatment was unknown.

Relevant test results included:

On 15-Apr-2025: blood glucose: high blood sugar (Ref range: not provided).

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

The outcome of blood glucose increased, chronic disease and condition aggravated was not recovered.

The reporter assessed the seriousness of blood glucose increased, chronic disease and condition aggravated as serious (hospitalization).

The reporter did not provide the causality of blood glucose increased, chronic disease and condition aggravated in relationship to Eligard and Eligard Unspecified Device.

On 12-May-2025, follow up information was received by Adium via Patient Support Program (reference number: PA-ADIUM-PA-0023-20250317) from a consumer (Patient's daughter/family member/ non-healthcare professional) and sent to Tolmar on 13-May-2025. New information included: Serious event of 'Hospitalized for multiple cerebral ischemias' (Cerebral ischaemia) (Life-threatening; disability; hospitalization) was added. Added new serious (hospitalisation) events of 'Fainting after ingestion of Xtandi' (Syncope), 'Blood pressure 64/34' (Hypotension), 'fever' (Pyrexia) and non-serious event 'due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May-2025 (Intentional dose omission), previous reported serious event Blood glucose increased - verbatim was updated High blood sugar from High blood sugar/ Sugar 225 and outcome was updated from not recovered to unknown and additional seriousness of hospitalisation was added . medical history was added Laboratory tests were added. Xtandi was updated to co-suspect.

Continuation Sheet for CIOMS report

Medical history included hypotension and blood glucose increased

On 09-Apr-2025, the patient was hospitalized due to multiple cerebral ischemia.

On an unknown date in 2025, during the hospitalization, the patient underwent CT scan and MRI. But through the MRI only he was confirmed for cerebral ischemia.

On 09-May-2025, the patient was discharged from the hospital.

On 12-May-2025, the patient was again hospitalized due to fever, low blood pressure, high sugar and due to fainting after ingestion of Xtandi.

On an unknown date in May-2025, the patient was intended to receive Eligard but due to his condition he was not able to apply Eligard dose that corresponded to the month.

The patients' daughter reported that patient continues with both treatments of Eligard and Xtandi, but she does not know when the last dose of Eligard was given as it was 6 months ago (Expiration date and lot number is not reported). She confirmed that the patient had already suffered from low blood pressure and high blood sugar before starting Eligard and Xtandi.

Further corrective treatment was reported.

Relevant test results included:

On an unknown date in 2025: CT scan: Unknown (Ref. range: Not provided).

On an unknown date in 2025: MRI: The patient was diagnosed with cerebral ischemia (Ref. range: Not provided).

On 12-May-2025: Blood glucose: Sugar 225 (Ref. range: Not provided).

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

The outcome of syncope, hypotension, blood glucose increased, cerebral ischaemia, pyrexia and intentional dose omission was unknown.

The reporter assesses the seriousness of syncope, hypotension, blood glucose increased, cerebral ischaemia, pyrexia as serious (hospitalisation) and did not assess for intentional dose omission.

The reporter did not provide the causality of syncope, hypotension, blood glucose increased, cerebral ischaemia, pyrexia, intentional dose omission in relationship to Eligard and Eligard unspecified device.

No further information is expected as the reporter did not consent to be contacted for follow-up.

Listedness:

Cerebral ischaemia >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024

Cerebral ischaemia > Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025

Cerebral ischaemia > Eligard®>unlisted as per USPI Eligard®>Feb-2025

Cerebral ischaemia > Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Chronic disease>Eligard>Unlisted as per CCDS>07-Nov-2024

Chronic disease>Eligard>Unlisted as per USPI>Feb-2025

Chronic disease>Eligard unspecified device>Unlisted as per USPI>Feb-2025

Chronic disease>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Condition aggravated>Eligard>Unlisted as per CCDS>07-Nov-2024

Condition aggravated>Eligard>Unlisted as per USPI>Feb-2025

Condition aggravated>Eligard unspecified device>Unlisted as per USPI>Feb-2025

Condition aggravated>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Pyrexia >Eligard® >listed as per CCDS Eligard®> 7-Nov-2024

Pyrexia> Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025

Pyrexia> Eligard®>unlisted as per USPI Eligard®>Feb-2025

Pyrexia> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Blood glucose increased>Eligard>listed as per CCDS>07-Nov-2024

Blood glucose increased>Eligard>listed as per USPI>Feb-2025

Blood glucose increased>Eligard unspecified device>listed as per USPI>Feb-2025

Blood glucose increased>Eligard>listed as per Canadian monograph>02-Apr-2025

Hypotension>Eligard® >listed as per CCDS Eligard®> 7-Nov-2024

Hypotension> Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025

Hypotension> Eligard®>listed as per USPI Eligard®>Feb-2025

Hypotension> Eligard® Unspecified Device> listed as per USPI Eligard®>Feb-2025

Continuation Sheet for CIOMS report

Syncope>Eligard® >listed as per CCDS Eligard®> 7-Nov-2024
 Syncope> Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025
 Syncope> Eligard®>listed as per USPI Eligard®>Feb-2025
 Syncope> Eligard® Unspecified Device> listed as per USPI Eligard®>Feb-2025

Intentional dose omission >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
 Intentional dose omission > Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
 Intentional dose omission > Eligard®>unlisted as per USPI Eligard®>Feb-2025
 Intentional dose omission > Eligard unspecified device>unlisted as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding an elderly 81-year-old male patient who experienced blood glucose increased (high blood sugar), chronic disease and condition aggravated (completely decompensated) during Eligard (leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed the reported event as serious (hospitalisation and medically significant) since the patient was hospitalised in response to events. The reported event blood glucose increased is assessed as not related Eligard (drug) considering the medical history of blood glucose increased, elderly age and co-existing events chronic disease completely decompensated. The events chronic disease and condition aggravated could not be assessed conclusively for events chronic disease and condition aggravated for drug Eligard due to lack of sufficient information regarding clinical details, exact condition that was decompensated, relevant medical history if any, concomitant medication details, lab reports if any. All the reported events were assessed as not related to device component of Eligard.

Fu added events Cerebral ischaemia (Hospitalized for multiple cerebral ischemias), Syncope (Fainting after ingestion of Xtandi), Hypotension (Blood pressure 64/34), Pyrexia (fever) and Intentional dose omission (due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May-2025). Tolmar assessed the event Cerebral ischaemia as serious (Life-threatening; disability; hospitalization) as it lead to hospitalisation, resulted in disability and life-threatening nature of the event, events syncope, hypotension, pyrexia resulted in hospitalisation and intentional dose omission was assessed as non-serious since it did not meet the ICH seriousness criteria.

The causality of event cerebral ischaemia was assessed as not related to suspect Eligard(drug and device) considering the nature of event, aetiopathogenesis and medical history of blood glucose increased prior to starting Eligard and advancing age could be risk factors for the event. The causality of event syncope was assessed as not related to suspect Eligard(drug and device) as per available information it occurred after ingestion of Xtandi. The causality of event hypotension and pyrexia was assessed as not related to suspect Eligard as hypotension could be due to coexisting events, patient had history of hypotension prior to starting Eligard which could be risk factor, pyrexia could be due to co-existing events, elderly age and immunosuppressed state of patient due to underlying prostate cancer could be risk factors. The causality of event intentional dose omission was assessed as not related to suspect Eligard(drug and device) as it is due to human action rather than due to drug.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
BLOOD GLUCOSE	15/Apr/2025		
BLOOD PRESSURE	12/May/2025		
CT SCAN	//2025		
MRI	//2025		
SUGAR	12/May/2025		

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

1) Test Name: BLOOD GLUCOSE

Result Unstructured Data (free text) : High blood sugar

Test Date: 15/Apr/2025

2) Test Name: BLOOD PRESSURE

Result Unstructured Data (free text) : Blood pressure 64/34

Test Date: 12/May/2025

3) Test Name: CT SCAN

Result Unstructured Data (free text) : Unknown

Test Date: //2025

Continuation Sheet for CIOMS report

4) Test Name: MRI

Result Unstructured Data (free text) : The patient was diagnosed with cerebral ischemia

Test Date: //2025

5) Test Name: SUGAR

Result Unstructured Data (free text) : Sugar 225

Test Date: 12/May/2025

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
 Lot Number : 1) Unknown
 Daily Dose : (45 milligram(s), 1 in 6 Month)
 Route of Admin : 1) Subcutaneous
 Indications : 1) Prostate cancer [10060862 - Prostate cancer]
 Therapy Dates : 1) From : 01/Apr/2024 To :Continuing
 Action(s) Taken With Drug : Dose not changed

Causality

- 1) Hospitalized for multiple cerebral ischemias (Cerebral ischemia - 10008121, Cerebral ischaemia - 10008120)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 2) Completely decompensated (Chronic disease - 10076311, Chronic disease - 10076311)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not assessable
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 3) Completely decompensated (Condition worsened - 10076326, Condition aggravated - 10010264)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not assessable
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 4) Fever (Fever - 10016558, Pyrexia - 10037660)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 5) High blood sugar/ Sugar 225 (Blood glucose increased - 10005557, Blood glucose increased - 10005557)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 6) Fainting after ingestion of Xtandi (Fainting - 10016169, Syncope - 10042772)
 Causality as per reporter : Not Related
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 7) Blood pressure 64/34 (Blood pressure low - 10005753, Hypotension - 10021097)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 8) due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May 2025, (Intentional dose omission - 10079221, Intentional dose omission - 10079221)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable

Labeling :

Continuation Sheet for CIOMS report

- 1) Hospitalized for multiple cerebral ischemias
CORE UnLabeled
 - 2) Completely decompensated
CORE UnLabeled
 - 3) Completely decompensated
CORE UnLabeled
 - 4) Fever
CORE Labeled
 - 5) High blood sugar/ Sugar 225
CORE Labeled
 - 6) Fainting after ingestion of Xtandi
CORE Labeled
 - 7) Blood pressure 64/34
CORE Labeled
 - 8) due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May 2025,
CORE UnLabeled
- 2) Drug : Eligard® Unspecified Device (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form of Admin : 1) Injection
Lot Number : 1) Unknown
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

- 1) Hospitalized for multiple cerebral ischemias (Cerebral ischemia - 10008121, Cerebral ischaemia - 10008120)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
- 2) Completely decompensated (Chronic disease - 10076311, Chronic disease - 10076311)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
- 3) Completely decompensated (Condition worsened - 10076326, Condition aggravated - 10010264)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
- 4) Fever (Fever - 10016558, Pyrexia - 10037660)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
- 5) High blood sugar/ Sugar 225 (Blood glucose increased - 10005557, Blood glucose increased - 10005557)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
- 6) Fainting after ingestion of Xtandi (Fainting - 10016169, Syncope - 10042772)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
- 7) Blood pressure 64/34 (Blood pressure low - 10005753, Hypotension - 10021097)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
- 8) due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May 2025, (Intentional dose omission - 10079221, Intentional dose omission - 10079221)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable

Continuation Sheet for CIOMS report

ReChallenge : Not Applicable

Labeling :

- 1) Hospitalized for multiple cerebral ischemias
CORE
- 2) Completely decompensated
CORE
- 3) Completely decompensated
CORE
- 4) Fever
CORE
- 5) High blood sugar/ Sugar 225
CORE
- 6) Fainting after ingestion of Xtandi
CORE
- 7) Blood pressure 64/34
CORE
- 8) due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May 2025,
CORE

- 3) Drug : XTANDI
Active Substance : 1) ENZALUTAMIDE
Drug Characterization : Suspect
Form Strength : 1) 40 Milligram
Form of Admin : 1) Capsule
Lot Number : 1) Unknown
2) Unknown
Daily Dose : (160 milligram(s), 1 in 1 Day)
Route of Admin : 1) Oral
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates : 1) From : 01/Apr/2024 To :Continuing
2) From : /May/2025 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

- 1) Hospitalized for multiple cerebral ischemias (Cerebral ischemia - 10008121, Cerebral ischaemia - 10008120)
Causality as per reporter : Not Reported
- 2) Completely decompensated (Chronic disease - 10076311, Chronic disease - 10076311)
Causality as per reporter : Not Reported
- 3) Completely decompensated (Condition worsened - 10076326, Condition aggravated - 10010264)
Causality as per reporter : Not Reported
- 4) Fever (Fever - 10016558, Pyrexia - 10037660)
Causality as per reporter : Not Reported
- 5) High blood sugar/ Sugar 225 (Blood glucose increased - 10005557, Blood glucose increased - 10005557)
Causality as per reporter : Not Reported
- 6) Fainting after ingestion of Xtandi (Fainting - 10016169, Syncope - 10042772)
Causality as per reporter : Not Reported
- 7) Blood pressure 64/34 (Blood pressure low - 10005753, Hypotension - 10021097)
Causality as per reporter : Not Reported
- 8) due to her condition she has not been able to apply her Eligard dose that corresponded to the month of May 2025, (Intentional dose omission - 10079221, Intentional dose omission - 10079221)
Causality as per reporter : Not Reported

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

Dosage Text :

Drug 1 :Eligard®

1) ELIGARD 45 MG x 1 LIO x 1 JER

Drug 3 :XTANDI

1) 40 milligram, qid XTANDI 40 MG x 120 CAP x 30 FND

23. OTHER RELEVANT HISTORY (Continuation...)

2) LOW BLOOD PRESSURE (10024895 , Low blood pressure) (Continuing : Unknown)

Continuation Sheet for CIOMS report

3) HIGH BLOOD SUGAR (10005557 , Blood glucose increased) (Continuing : Unknown)