SUSPECT ADVERSE REACTION REPORT

PA-TOLMAR, INC.-25PA056898

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
FJS	PANAMA	02	Dec	1939	85	Male		Jan	2025

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

1) Paralysis of hands and feet/currently cannot move his hands or feet, difficulty swallowing, speak little (Paralysis (10033799), Paralysis (10033799))
Not Recovered/Not Resolved/Ongoing
2) stroke (Stroke (10042244), Cerebrovascular accident (10008190))
(/Jan/2025 -) - Not Recovered/Not Resolved/Ongoing
3) The patient was unable to attend his scheduled appointment on 22-jan-2025 for due Eligard application as urologist had not contacted (Intentional deviation from dosage regimen (10080008), Intentional product use issue (10076308))
(12/Jan/2025 -) - Unknown

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ 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)(Unknown)

Cont..

15. DAILY DOSE(S)

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

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

Cont..

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous
2) Subcutaneous

Cont..

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

Cont..

18. THERAPY DATE(S) (from/to)

1) (01/Dec/2023 - ONGOING)

19. THERAPY DURATION

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

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

(NA : Not Applicable)

III. CONCOMITANT DRUG(S) AND HISTORY

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

1)OTHER THERAPEUTIC PRODUCTS(Medication to strengthen bones)

Cont..

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

1) PHYSICAL THERAPY (10050334, Physical therapy) (20/Feb/2025 -) (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.: NA
Center No.:
Subject Id :

24.REPORT NULLIFIED ☐ YES ☐ NO

24b. MFR CONTROL NO.

PA-TOLMAR, INC.-25PA056898

24c. DATE RECEIVED BY MANUFACTURER

16/Apr/2025

24d. REPORT SOURCE ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL

DATE OF THIS REPORT

26/Apr/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...)

Event Description :

This Study report from PANAMA was received by Adium via PSP (Patient Support Program)-Prevenfuturo (reference number: PA-ADIUM-PA-0008-20250217) on 17-FEB-2025 from a Consumer/Other Non-Health Prof regarding an Elderly 85 Years old Male patient who experienced serious (Hospitalization, Disability) event of stroke (Stroke), serious (Hospitalization, Disability, Medically Significant) event Paralysis of hands and feet/ currently cannot move his hands or feet, Difficulty swallowing, Speak little (Paralysis), non-serious event the patient was unable to attend his scheduled appointment on 22-JAN-2025 for due Eligard application as urologist had not contacted (Intentional deviation from dosage regimen), during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. The needle component of the constituent device was not identified in the report. Xtandi (enzalutamide) was also considered as suspect. The report was sent to Tolmar on 18-FEB-2025.

The patient's medical history and current conditions included Prostate cancer, Metastases to bone, Pain in hip, Gastrointestinal tube insertion.

Concomitant medications included unspecified medication to strengthen bones and unspecified medications for hip pain.

On 29-NOV-2023 (as per CRM (customer relationship management system) start date was 01-DEC-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 an unspecified date, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (around the navel) (Lot numbers and Expiration dates not provided). The patient's last dose of Xtandi was on 02-JAN-2025. On an unspecified date, the patient was hospitalized for one month due to a stroke, and as a result, the patient currently could not move his hands or feet, difficulty swallowing, and speak little. On an unspecified date (15 days ago from date of report), the patient underwent a gastro procedure (unspecified) and for this reason, the patient must eat via a tube placed in his stomach. The patient's son wants to consult about how the patient with difficulty swallowing, might take enzalutamide pill. The patient's son was not aware of how severe the stroke would be and consequently, the patient was unable to attend his scheduled appointment on 22-JAN-2025 as due for his Eligard application. Since the patient was discharged, the urologist has not contacted the patient's son, despite his attempts to reach him.

Corrective treatment was not reported.

Action taken with Eligard in response to the events was Dose Not Changed. De-challenge was not applicable, and re-challenge was not applicable.

The outcome of Paralysis was Not Recovered.

The outcome of Stroke was Not Recovered.

The outcome of Intentional deviation from dosage regimen was Unknown.

The reporter assessed the seriousness of Stroke, and Paralysis as serious (Hospitalized, Disability), did not assess for remaining events and did not assess the causality in relationship to Eligard.

On 03-Apr-2025, follow-up information was received by Adium (reference number: PA-ADIUM-PA-0008-20250217) from a consumer (Patient's son) (non-healthcare professional) and sent to Tolmar on 05-Apr-2025. New information included: event onset date added for stroke. Date of hospitalization added. Concomitant medication added as Omacor, Norvasc, other therapeutic products (Eye drop), other therapeutic products (Bone medication) and other therapeutic products (vitamins). Medical history added as Blood pressure increased, Mobility decreased, Physical therapy and Deterioration of visual acuity. The seriousness criteria for the serious (Hospitalization, Disability) event Paralysis of hands and feet/currently cannot move his hands or feet, Difficulty swallowing, speak little (Paralysis) updated.

The patient's past medical history was unknown and current condition Prostate cancer, Gastrointestinal tube insertion, Metastases to bone, Pain in hip, Blood pressure increased, Mobility decreased, Physical therapy and Deterioration of visual acuity.

Concomitant drug included Omacor(Omega-3-Acid Ethyl Ester), Norvasc (Amlodipine Besilate), other therapeutic products (Eye drop), other therapeutic products (Bone medication) and other therapeutic products (vitamins).

On 29-Nov-2023, the patient began taking Xtandi capsules (160 mg, once daily). The According to the reporter, the lot number of the medication taken at the time the event began was unknown. The patient consistently continued the Xtandi regimen, only interrupting it during a brief hospitalization from December 12-Jan-2025 to 02-Feb-2025. Reporter did not provide copies of laboratory or diagnostic test results and was unsure whether Xtandi contributed to the stroke, as doctors have not indicated any causal relationship. No further details were available.

On an unspecified date of Jan-2025, the patient had stroke. Following the stroke, the patient underwent the placement of a gastrostomy tube for feeding by the Urological Center between late January and early Feb-2025, due to difficulty swallowing physical therapy was initiated on 20-Feb-2025 and continues three times a week. The patient was also receiving physical therapy twice a week prior to the stroke due to age-related mobility deterioration. No further details were available.

Corrective treatment was not reported.

Action taken with Eligard in response to the event was Dose Not Changed. De-challenge and re-challenge were not applicable.

The outcome of Stroke was Not Recovered/Not Resolved.

Continuation Sheet for CIOMS report

The reporter did not assess the seriousness of stroke.

The reporter did not provide the causality of stroke in relation to Eligard and Eligard Unspecified Device.

On 16-Apr-2025, follow up information was received via Adium (reference number: PA-ADIUM-PA-0008-20250217) from a consumer (patient's wife and son (non-healthcare professional) and sent to Tolmar on 16-Apr-2025. New information included: a new dose of Xtandi (enzalutamide) was added. Narrative was updated.

On an unknown date in March-2025, the patient resumed Xtandi (enzalutamide).

On an unknown date, the patient was bedridden at home due to the stroke and cannot swallow or chew, for that reason his medicines were given with special milk by means of a bottle.

Listedness of the events paralysis, cerebrovascular accident and intentional product use issue are retained as per previous assessment.

Company Remarks (Sender's Comments) :

Evaluator Comment (Tolmar): This 85 years old male patient had Paralysis (Paralysis of hands and feet/currently cannot move his hands or feet), Cerebrovascular accident (Stroke) and Intentional product use issue (The patient was unable to attend his scheduled appointment on 22-JAN-2025 for due Eligard application as urologist had not contacted) during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. Xtandi (enzalutamide) was also considered as suspect. Tolmar maintained seriousness of Paralysis and Cerebrovascular accident as hospitalization and disability, while Intentional product use issue as non-serious since it did not meet ICH seriousness criteria. Intentional product use issue was not related to Eligard (drug and device) as it was due to human action. Cerebrovascular accident was assessed as related to Eligard drug (unrelated to device) based on temporal relation and known safety profile of the drug. Confounder- co-suspect Xtandi and malignancy due to associated hypercoagulable state. Risk factor- elderly age. Paralysis was post-stroke hence assessed as not related to Eligard (drug and device).

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
Lot Number	:	1) Unknown 2) Unknown
Daily Dose	:	(45 milligram(s), 1 in 6 Month) (45 milligram(s), 1 in 6 Month)
Route of Admin	:	1) Subcutaneous 2) Subcutaneous
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	1) From : 01/Dec/2023 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) Paralysis of hands and feet/currently cannot move his hands or feet, difficulty swallowing, speak little (Paralysis - 10033799, Paralysis - 10033799)

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

2) stroke (Stroke - 10042244, Cerebrovascular accident - 10008190)

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

3) The patient was unable to attend his scheduled appointment on 22-jan-2025 for due Eligard application as urologist had not contacted (Intentional deviation from dosage regimen - 10080008, Intentional product use issue - 10076308)

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) Paralysis of hands and feet/currently cannot move his hands or feet, difficulty swallowing, speak little
CORE UnLabeled
2) stroke
CORE Labeled
3) The patient was unable to attend his scheduled appointment on 22-jan-2025 for due Eligard application as urologist had not contacted
CORE UnLabeled

2) Drug : Eligard® Unspecified Device (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) Paralysis of hands and feet/currently cannot move his hands or feet, difficulty swallowing, speak little (Paralysis - 10033799, Paralysis - 10033799)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) stroke (Stroke - 10042244, Cerebrovascular accident - 10008190)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) The patient was unable to attend his scheduled appointment on 22-jan-2025 for due Eligard application as urologist had not contacted (Intentional deviation from dosage regimen - 10080008, Intentional product use issue - 10076308)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Paralysis of hands and feet/currently cannot move his hands or feet, difficulty swallowing, speak little
CORE
2) stroke
CORE
3) The patient was unable to attend his scheduled appointment on 22-jan-2025 for due Eligard application as urologist had not contacted
CORE

3) Drug : XTANDI
Active Substance : 1) ENZALUTAMIDE
Drug Characterization : Suspect
Form of Admin : 1) Capsule
2) Capsule
3) Capsule
4) Capsule
Lot Number : 1) Unknown
2) Unknown
3) Unknown
4) Unknown
Daily Dose : (40 milligram(s), in 1 Day)
(160 milligram(s), 1 in 1 Day)
Route of Admin : 1) Oral
2) Oral
3) Oral
4) Oral
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates : 1) From : 29/Nov/2023 To :12/Jan/2025
2) From : 01/Dec/2023 To :Continuing
3) From : 12/Feb/2025 To :Continuing
4) From : /Mar/2025 To :Continuing
Therapy Duration : 1) 411 Days
Action(s) Taken With Drug : Dose not changed

Causality

Continuation Sheet for CIOMS report

1) Paralysis of hands and feet/currently cannot move his hands or feet, difficulty swallowing, speak little (Paralysis - 10033799, Paralysis - 10033799)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) stroke (Stroke - 10042244, Cerebrovascular accident - 10008190)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) The patient was unable to attend his scheduled appointment on 22-jan-2025 for due Eligard application as urologist had not contacted (Intentional deviation from dosage regimen - 10080008, Intentional product use issue - 10076308)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

2) 45 milligram, q 6 month

Drug 2 :Eligard® Unspecified Device

1) UNK

Drug 3 :XTANDI

1) 4 capsules of 40 mg per day (160 mg per day)

4) XTANDI 40 MG x 120 CAP x 30 FND

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

1). Drug : OTHER THERAPEUTIC PRODUCTS
Active Substance : 1) Medication to strengthen bones
Form Strength :
Daily Dose : 1) (in 6 Month)
Indications : 1) strengthen his bones [10066215 - Supplementation therapy]
Dosage Text : 1) UNK, q 6 month

2). Drug : OTHER THERAPEUTIC PRODUCTS
Active Substance : 1) Medications for hip pain
Form Strength :
Indications : 1) hip pain [10003239 - Arthralgia]
Dosage Text : 1) UNK

3). Drug : Omacor
Active Substance : 1) OMEGA-3-ACID ETHYL ESTER
Form Strength :
Indications : 1) Product used for unknown indication [10070592 - Product used for unknown indication]

4). Drug : Norvasc
Active Substance : 1) AMLODIPINE BESILATE
Form Strength :
Indications : 1) Product used for unknown indication [10070592 - Product used for unknown indication]

5). Drug : OTHER THERAPEUTIC PRODUCTS
Active Substance : 1) eye drops
Form Strength :
Indications : 1) Product used for unknown indication [10070592 - Product used for unknown indication]

Continuation Sheet for CIOMS report

6). Drug	:	OTHER THERAPEUTIC PRODUCTS
Active Substance	:	1) Bone medication
Form Strength	:	
Indications	:	1) Product used for unknown indication [10070592 - Product used for unknown indication]

7). Drug	:	OTHER THERAPEUTIC PRODUCTS
Active Substance	:	1) vitamins
Form Strength	:	
Indications	:	1) Product used for unknown indication [10070592 - Product used for unknown indication]

23. OTHER RELEVANT HISTORY (Continuation...)

2) PROSTATE CANCER (10060862 , Prostate cancer) (Continuing : YES)

3) INSERTION OF FEEDING TUBE (10053050 , Gastrointestinal tube insertion) (Continuing : YES)

4) METASTASES TO BONE (10027452 , Metastases to bone) (Continuing : YES)

5) PAIN IN HIP (10033432 , Pain in hip) (Continuing : YES)

6) HIGH PRESSURE (10005750 , Blood pressure increased) (Continuing : YES)

7) LOSING MOBILITY (10048334 , Mobility decreased) (Continuing : YES)

8) DETERIORATION OF HER BODY (10012546 , Deterioration of visual acuity) (Continuing : YES)