SUSPECT ADVERSE REACTION REPORT

PA-TOLMAR, INC.-23PA040808

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
M-V	PANAMA	06	Mar	1929	94	Male	28	Mar	2025

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

1) death (Death (10011906), Death (10011906))
Fatal
2) Mobility decreased (Mobility decreased (10048334), Mobility decreased (10048334))
(28/Mar/2025 -) - Not Recovered/Not Resolved/Ongoing
3) Hip fracture (Hip fracture (10020100), Hip fracture (10020100))
Not Recovered/Not Resolved/Ongoing
4) the patient is bedridden/bedridden (Bedridden (10048948), Bedridden (10048948))
Not Recovered/Not Resolved/Ongoing

Cont..

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [x] PATIENT DIED
- [ ] LIFE THREATENING
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [x] 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)

Cont..

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
1) (45 milligram(s), 1 in 6 Month)	1) 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
1) (21/May/2021 - ongoing)	

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
Anjan.Chatterjee@tolmar.comand+1--9702124900

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

24.REPORT NULLIFIED	24b. MFR CONTROL NO.
☐ YES ☐ NO	PA-TOLMAR, INC.-23PA040808
24c. DATE RECEIVED BY MANUFACTURER: 17/Jul/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 22/Jul/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) Given an injection to strengthen the bones (Bone disorder (10005956), Bone disorder (10005956) - Not Recovered/Not Resolved/Ongoing)

6) Leg atrophy (Muscle atrophy (10028289), Muscle atrophy (10028289)(28/Mar/2025 -) - Not Recovered/Not Resolved/Ongoing)

7) He has lost the clarity of thought (Thinking abnormal (10043431), Thinking abnormal (10043431) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from PANAMA was received by Adium (reference number: PA-0131-20230511) via Patient Support Program "ASOFARMA A TU LADO" on 10-MAY-2023 from a Consumer/Other Non-Health Prof regarding an Elderly 94 Years old Male patient who experienced medically significant event of hip fracture (Hip fracture), given an injection to strengthen the bones (Bone disorder), disability event of the patient is bedridden (Bedridden) and non-serious event of he has lost the clarity of thought (Thinking abnormal), 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 11-MAY-2023.

The patient's medical history and current conditions included Prostate cancer.

Concomitant medications were not reported.

On an unspecified date, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Batch details not provided). It was reported that the patient was bedridden (onset date unknown). Patient suffered a hip fracture (onset date unknown) and a month ago the patient had a bone density scan and was given an injection to strengthen the bones. It was unknown if the patient already suffered bone disease before Eligard. His daughter was in control of the medication because he has lost the clarity of thought (onset date unknown). No further details were provided. Corrective treatment was not reported. Action taken with Eligard in response to the events was Unknown. De-challenge was Not applicable, and re-challenge was Not applicable. The outcome of Hip fracture was Not Recovered/Not Resolved. The outcome of Bedridden was Not Recovered/ Not Resolved. The outcome of Bone disorder was Unknown. The outcome of Thinking abnormal was Unknown.

Relevant test results included:
Unknown date: Bone scan: results not provided.

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

On 22-MAY-2023, follow-up information was received by Adium (reference number: PA-0131-20230511) and sent to Tolmar on 22-MAY-2023. It was informed that there was no answer to call made to reporter, and no further information was provided. Since no new information was provided, this follow up was considered non-significant.

On 20-JUN-2023, follow-up information was received by Adium (reference number: PA-0131-20230511) which include query attempts and sent to Tolmar on 20-JUN-2023. No new information was provided. This follow up was considered non-significant.

On 18-JUL-2023, follow-up information was received by Adium (reference number: PA-0131-20230511) which include query attempts and sent to Tolmar on 19-JUL-2023. No new information was provided. Since no new information was provided, this follow up was considered non-significant.

On 17-AUG-2023, follow-up information was received by Adium (reference number: PA-0131-20230511) which included unsuccessful follow up attempt and sent to Tolmar on 17-AUG-2023. Since no new information was provided this follow up was considered non-significant.

On 02-Apr-2025, follow-up information was received via Adium (reference number: PA-0131-20230511) from a Consumer family member (non-healthcare professional) and sent to Tolmar on 03-Apr-2025. New information included: Eligard dose added. New serious event (Disability) added as “Mobility decreased” (Mobility decreased), and non-serious events of “Leg atrophy” (Muscle atrophy). New seriousness criteria of disability added for event hip fracture. Events verbatim updated from “the patient is bedridden” to “the patient is bedridden/bedridden”. Therapy start date for Eligard treatment added.

On 21-May-2021, the patient began receiving Eligard 45 mg, every 6 months, via subcutaneous route for prostate cancer (Lot number and Expiration dates were not reported).

On 28-Mar -2025, the patient had lost a significant amount of mobility due to being bedridden, and his legs had experienced quite a lot of atrophy. No further details were available.

Corrective treatment was unknown.

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

The outcome of mobility decreased, and muscle atrophy was not recovered.

The reporter did not assess the seriousness of mobility decreased and muscle atrophy.

The reporter did not provide the causality of mobility decreased and muscle atrophy in relationship to Eligard and Eligard Unspecified device.

Continuation Sheet for CIOMS report

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

On 17-Jul-2025, the follow-up information was received via Adium (reference number: PA-0131-20230511 (4)) from a Consumer family member (non-healthcare professional) and sent to Tolmar on 18-Jul-2025. New information included: Added a new serious event of death (death). Action taken updated from 'dose not changed' to 'not applicable'. Narrative was updated.

On an unknown date, the patient died due to unknown cause of death. The patient was 96-year-old at the time of his death. It was unknown if an autopsy was performed. No further details were available.

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

The outcome of death was fatal.

The reporter assessed the seriousness of death as serious (death).

The reporter assessed the causality of death in relationship to Eligard and Eligard unspecified device as not related.

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

Listedness for events hip fracture, bedridden, bone disorder and thinking abnormal were retained as per previous assessment.

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

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

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

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding a 94-year-old male patient who experienced hip fracture (Hip fracture), patient is bedridden (Bedridden), bone disorder (given an injection to strengthen the bones) and thinking abnormal (he has lost the clarity of thought) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed the event hip fracture (medically significant and disability) and bone disorder as serious (medically significant) as hip fracture requires significant medical intervention to prevent a serious outcome and can jeopardize the patient and bone disorder is considered serious due to the injection patient received for strengthening bone. Patient is bedridden is considered serious (disability) as it has a significant impact on the quality of life of the patient and consequences can be jeopardizing. Thinking abnormal is considered as non-serious since there is no immediate jeopardy and the event did not meet ICH seriousness criteria. All the events are considered as not related to Eligard (drug and device). Circumstances of hip fracture is not provided (fall could be likely reason as they are common in elderly age population) and there is on reasonable evidence to attribute its causal association with Eligard. Patient is bedridden is attributable to concurrent hip fracture as mentioned in the narrative, hence the event is considered as not related to Eligard. Bone disorder is considered as not related to Eligard as the information provided is limited and more information is needed for comprehensive medical assessment of the case. Advanced age of the patient is a strong confounder for bone disorder and hip fracture as it is associated with age-related degenerative bone changes. Thinking abnormal is attributable to advanced age of the patient and not related to Eligard.

FU - added events of mobility decreased (Mobility decreased) and muscle atrophy (Leg atrophy) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed the event mobility decreased as serious as it resulted in disability. Event muscle atrophy was assessed as non-serious since it does not meet the ICH seriousness criteria and is not an IME event. Event mobility decreased and muscle atrophy were assessed as not related to Eligard (drug and device) as the events can be explained by patient being reported with hip fracture and being bedridden. Elderly age of the patient could be the possible risk factor for the reported events.

FU - Event Death (Death) was added on follow-up. Tolmar assessed the event as serious (Fatal). The reported fatal event death was considered as not assessable to Eligard (drug) and not related to device considering limited information regarding events leading to death, autopsy details, cause of death. Patient's elderly age and underlying prostate cancer could be contributing factors.

Additional Information (Continuation...)

Lab Result :

Continuation Sheet for CIOMS report

Test Name	Test Date	Test Result	Normal Value
BONE DENSITY SCAN	Unknown		

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

1) Test Name: BONE DENSITY SCAN

Result Unstructured Data (free text) : results not provided

Test Date: Unknown

Lab Comments :

1) Test Name : BONE DENSITY SCAN

Lab Comments : results not provided

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 : 21/May/2021 To :Not applicable
Action(s) Taken With Drug : Not applicable

Causality

1) death (Death - 10011906, Death - 10011906)
Causality as per reporter : Not Related
Causality as per Mfr : Not assessable
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Mobility decreased (Mobility decreased - 10048334, Mobility decreased - 10048334)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Hip fracture (Hip fracture - 10020100, Hip fracture - 10020100)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) the patient is bedridden/bedridden (Bedridden - 10048948, Bedridden - 10048948)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) Given an injection to strengthen the bones (Bone disorder - 10005956, Bone disorder - 10005956)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) Leg atrophy (Muscle atrophy - 10028289, Muscle atrophy - 10028289)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) He has lost the clarity of thought (Thinking abnormal - 10043431, Thinking abnormal - 10043431)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Continuation Sheet for CIOMS report

Labeling :

1) death
CORE UnLabeled
2) Mobility decreased
CORE UnLabeled
3) Hip fracture
CORE UnLabeled
4) the patient is bedridden/bedridden
CORE UnLabeled
5) Given an injection to strengthen the bones
CORE UnLabeled
6) Leg atrophy
CORE UnLabeled
7) He has lost the clarity of thought
CORE UnLabeled

2) Drug : Eligard® Unspecified Device (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) death (Death - 10011906, Death - 10011906)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Mobility decreased (Mobility decreased - 10048334, Mobility decreased - 10048334)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) Hip fracture (Hip fracture - 10020100, Hip fracture - 10020100)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) the patient is bedridden/bedridden (Bedridden - 10048948, Bedridden - 10048948)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
5) Given an injection to strengthen the bones (Bone disorder - 10005956, Bone disorder - 10005956)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
6) Leg atrophy (Muscle atrophy - 10028289, Muscle atrophy - 10028289)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
7) He has lost the clarity of thought (Thinking abnormal - 10043431, Thinking abnormal - 10043431)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) death
CORE
2) Mobility decreased
CORE
3) Hip fracture

Continuation Sheet for CIOMS report

CORE
4) the patient is bedridden/bedridden
CORE
5) Given an injection to strengthen the bones
CORE
6) Leg atrophy
CORE
7) He has lost the clarity of thought
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

Drug 2 :Eligard® Unspecified Device

1) UNK