SUSPECT ADVERSE REACTION REPORT

PA-TOLMAR, INC.-23PA041695

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
RGH	PANAMA	25	Jul	1935	87	Male		Jan	2024

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

1) DEHYDRATION (Dehydration (10012174), Dehydration (10012174))
Not Recovered/Not Resolved/Ongoing
2) Obstructed urethra (Urethral obstruction (10046459), Urethral obstruction (10046459))
Unknown
3) could not urinate due to infection (Urinary retention (10046555), Urinary retention (10046555))
Unknown
4) Urinary tract infection (Urinary tract infection (10046571), Urinary tract infection (10046571))
(/May/2025 -) - Recovering/Resolving

Cont..

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)(L15276CUY)

Cont..

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

15. DAILY DOSE(S)

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

Cont..

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous

Cont..

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

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

Cont..

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (13/Oct/2022 - 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)

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	24b. MFR CONTROL NO.
☐ YES ☐ NO	PA-TOLMAR, INC.-23PA041695
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
04/Jun/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
14/Jun/2025	☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) DIARRHEA (Diarrhea (10012727), Diarrhoea (10012735) - Not Recovered/Not Resolved/Ongoing)

6) IS NOW IN BED, WHERE ALL HIS DAILY NEEDS MUST BE TAKEN CARE OF (Activities of daily living impaired (10050954), Loss of personal independence in daily activities (10079487)(/Jan/2024 -) - Not Recovered/Not Resolved/Ongoing)

7) LOSS OF MUSCLE TONE (Hypotonia (10021118), Hypotonia (10021118)(/Jan/2024 -) - Not Recovered/Not Resolved/Ongoing)

8) A LOT OF WEAKNESS WHEN WALKING (Weakness (10047862), Asthenia (10003549) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from PANAMA was received by Adium (reference number: PA-0145-20230628) on 28-JUN-2023 from a Patient Family Member regarding an Elderly 87 Years old Male patient who was hospitalized due to Dehydration (Dehydration) and Diarrhea (Diarrhea), during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. The needle component of the constituent device was not identified in the report. XTANDI, capsules 40 mg, was also considered as suspect. The report was sent to Tolmar on 28-JUN-2023.

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

Concomitant medications were not reported.

On an unknown date, the patient began receiving Eligard 45 milligram, q 6 month, via Subcutaneous use for Prostate cancer (Batch details were not provided). It was informed that the patient had diarrhea for a week, and the patient was taken to the hospital in an emergency because of dehydration due to diarrhea (onset unknown). The patient's wife indicated that he continues with the symptoms mentioned above. It was informed had not been able to make an appointment with the urologist because of the patient's current diarrhea. No further details were provided.

Corrective treatment was not reported.

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

Action taken with XTANDI in response to the event was unknown. De-challenge was Not applicable, and re-challenge was Not applicable.

The outcome of Dehydration was Not Recovered/Not Resolved. The outcome of Diarrhea was Not Recovered/Not Resolved.

The reporter assessed the seriousness of Dehydration and Diarrhea as serious (Hospitalization) and assessed the causality in relationship to Eligard as Not Reported.

On 25-JUL-2023, follow-up information was received by Adium (reference number: PA-0145-20230628) from a Patient Family Member and sent to Tolmar on 26-JUL-2023. New information included non-serious event of a lot of weakness when walking (Weakness) and clinical course details.

It was reported that the patient had not been using XTANDI 160 mg, qd for 2 weeks by medical decision. the medication caused a lot of diarrhea (previously reported) and this symptom caused a lot of weakness when walking (onset date unknown). Patient discontinued XTANDI and continue with Eligard treatment. No further details were provided. Corrective treatment was not reported.

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

Action taken with XTANDI in response to the event was drug withdrawn. De-challenge was Not applicable, and re-challenge was Not applicable.

The outcome of Weakness was Not Recovered/Not Resolved.

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

No further information is expected as consent to be contacted was not provided.

On 20-MAR-2024, follow-up information was received by Aadium (reference number: PA-0145-20230628) from a Consumer/Other Non-Health Prof and sent to Tolmar on 21-MAR-2024. New information included the non-serious events of Loss of muscle tone (Hypotonia), is now in bed, where all his daily needs must be taken care of (Activities of daily living impaired) and case course details.

On JAN-2024, after the most recent dose of Eligard, the patient experienced Loss of muscle tone and was now in bed, where all his daily needs must be taken care of. No further details were provided.

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 Hypotonia was Not Recovered/Not Resolved. The outcome of Activities of daily living impaired was Not Recovered/Not Resolved.

Continuation Sheet for CIOMS report

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

Evaluator comment (Tolmar): This is regarding an elderly male patient who experienced dehydration (Dehydration) and diarrhea (Diarrhea) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. XTANDI, capsules 40 mg is also considered as suspect. Tolmar maintained both the events as serious due to hospitalization. As per the limited information provided (start date of suspect therapy and event onset dates are not provided, relevant medical history and clinical context is not provided) both the events are considered as not related to Eligard (drug and device). Dehydration is secondary to diarrhea as per the case context. Co-suspect XTANDI may have contributory role for both the events reported.

As per the follow up information provided patient experienced asthenia (a lot of weakness when walking). Tolmar assessed the event as non-serious since there is no immediate jeopardy and event did not meet ICH seriousness criteria. Based on the information available asthenia is attributable to concurrent diarrhea and not related to Eligard (drug and device). Elderly age and underlying prostate cancer are considered as confounding factors. Patient experienced hypotonia (loss of muscle tone) and loss of personal independence in daily activities (is now in bed, where all his daily needs must be taken care of). Tolmar assessed the both the events are considered as non-serious as they did not meet ICH seriousness criteria. As per the case context and product safety profile both the events are not attributable to Eligard (drug and device) hence considered as not related to Eligard. Elderly age and underlying prostate cancer are strong confounding factors.

On 04-Jun-2025, follow-up information was received by Aadium (reference number: PA-0145-20230628) from a consumer (non-healthcare professional) and sent to Tolmar on 05-Jun-2025. New information included: New serious events of "Urinary tract infection" (Urinary tract infection) (hospitalization), "obstructed urethra" (Urethral obstruction) (hospitalization) and "could not urinate due to infection" (Urinary retention) (hospitalization and disability). Eligard start date, batch/lot number and expiration dates added. Treatment added.

On 13-Oct-2022, the patient began receiving Eligard 45 mg, every 6 months, via subcutaneous route for prostate cancer (Lot number: L15276CUY; UNK; UNK and Expiration dates: Aug-2026; UNK; UNK).

On an unknown date, the patient urethra became obstructed and was unable to urinate.

On an unknown date in May-2025, the patient experienced severe urinary tract infection and was hospitalized for 12 days. This infection became complicated because his urethra became obstructed and he required bladder surgery to be able to urinate, as he was unable to urinate due to the infection.

Correction treatment included antibiotic treatment in hospital for urinary tract infection and bladder surgery in order to be able to urinate.

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

The outcome of urinary tract infection was recovering and urethral obstruction, urinary retention was unknown.

The reporter assessed the seriousness of urinary tract infection (hospitalization), urethral obstruction (hospitalization) and urinary retention (hospitalization and disability) as serious.

The reporter did not provide the causality of urinary tract infection, urethral obstruction, urinary retention 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.

On 05-Jun-2025, follow-up information was received by Aadium (reference number: PA-0145-20230628) and sent to Tolmar on 06-Jun-2025. No new information received.

Listedness:

Urinary tract infection>Eligard>Unlisted as per CCDS>07-Nov-2024
Urinary tract infection>Eligard>Unlisted as per USPI>Feb-2025
Urinary tract infection>Eligard® Unspecified Device>Unlisted as per USPI>Feb-2025
Urinary tract infection>Eligard>Listed as per Canadian monograph>02-Apr-2025

Urethral obstruction>Eligard>Unlisted as per CCDS>07-Nov-2024
Urethral obstruction>Eligard>Unlisted as per USPI>Feb-2025
Urethral obstruction>Eligard® Unspecified Device>Unlisted as per USPI>Feb-2025
Urethral obstruction>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Urinary retention>Eligard>Listed as per CCDS>07-Nov-2024
Urinary retention>Eligard>Listed as per USPI>Feb-2025
Urinary retention>Eligard® Unspecified Device>Listed as per USPI>Feb-2025
Urinary retention>Eligard>Listed as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Continuation Sheet for CIOMS report

Evaluator comment (Tolmar): This is regarding an elderly male patient who experienced dehydration (Dehydration) and diarrhea (Diarrhea) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. XTANDI, capsules 40 mg is also considered as suspect. Tolmar maintained both the events as serious due to hospitalization. As per the limited information provided (start date of suspect therapy and event onset dates are not provided, relevant medical history and clinical context is not provided) both the events are considered as not related to Eligard (drug and device). Dehydration is secondary to diarrhea as per the case context. Co-suspect XTANDI may have contributory role for both the events reported.
As per the follow up information provided patient experienced asthenia (a lot of weakness when walking). Tolmar assessed the event as non-serious since there is no immediate jeopardy and event did not meet ICH seriousness criteria. Based on the information available asthenia is attributable to concurrent diarrhea and not related to Eligard (drug and device). Elderly age and underlying prostate cancer are considered as confounding factors. Patient experienced hypotonia (loss of muscle tone) and loss of personal independence in daily activities (is now in bed, where all his daily needs must be taken care of). Tolmar assessed the both the events are considered as non-serious as they did not meet ICH seriousness criteria. As per the case context and product safety profile both the events are not attributable to Eligard (drug and device) hence considered as not related to Eligard. Elderly age and underlying prostate cancer are strong confounding factors.

Follow up - As per company conventions, events "Urinary tract infection" (Urinary tract infection) (hospitalization), Urethral obstruction ("obstructed urethra") (hospitalization) and Urinary retention ("could not urinate due to infection") (hospitalization and disability) are serious. Event Urinary retention is listed as per CCDS, USPI and Canadian monograph and event Urinary tract infection is listed in Canadian monograph, and unlisted as per CCDS and USPI. Event Urethral obstruction is unlisted. Events are assessed with not related causality.

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) L15276CUY
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 : 13/Oct/2022 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) DEHYDRATION (Dehydration - 10012174, Dehydration - 10012174)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Obstructed urethra (Urethral obstruction - 10046459, Urethral obstruction - 10046459)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) could not urinate due to infection (Urinary retention - 10046555, Urinary retention - 10046555)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Urinary tract infection (Urinary tract infection - 10046571, Urinary tract infection - 10046571)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) DIARRHEA (Diarrhea - 10012727, Diarrhoea - 10012735)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) IS NOW IN BED, WHERE ALL HIS DAILY NEEDS MUST BE TAKEN CARE OF (Activities of daily living impaired - 10050954, Loss of personal independence in daily activities - 10079487)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) LOSS OF MUSCLE TONE (Hypotonia - 10021118, Hypotonia - 10021118)

Continuation Sheet for CIOMS report

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

8) A LOT OF WEAKNESS WHEN WALKING (Weakness - 10047862, Asthenia - 10003549)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) DEHYDRATION
CORE UnLabeled
2) Obstructed urethra
CORE UnLabeled
3) could not urinate due to infection
CORE Labeled
4) Urinary tract infection
CORE UnLabeled
5) DIARRHEA
CORE Labeled
6) IS NOW IN BED, WHERE ALL HIS DAILY NEEDS MUST BE TAKEN CARE OF
CORE UnLabeled
7) LOSS OF MUSCLE TONE
CORE UnLabeled
8) A LOT OF WEAKNESS WHEN WALKING
CORE Labeled

2) Drug : Eligard® Unspecified Device (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form of Admin : 1) Injection
Lot Number : 1) L15276CUY
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

1) DEHYDRATION (Dehydration - 10012174, Dehydration - 10012174)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Obstructed urethra (Urethral obstruction - 10046459, Urethral obstruction - 10046459)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) could not urinate due to infection (Urinary retention - 10046555, Urinary retention - 10046555)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Urinary tract infection (Urinary tract infection - 10046571, Urinary tract infection - 10046571)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) DIARRHEA (Diarrhea - 10012727, Diarrhoea - 10012735)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) IS NOW IN BED, WHERE ALL HIS DAILY NEEDS MUST BE TAKEN CARE OF (Activities of daily living impaired - 10050954, Loss of personal independence in daily activities - 10079487)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable

Continuation Sheet for CIOMS report

ReChallenge : Not Applicable

7) LOSS OF MUSCLE TONE (Hypotonia - 10021118, Hypotonia - 10021118)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

8) A LOT OF WEAKNESS WHEN WALKING (Weakness - 10047862, Asthenia - 10003549)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) DEHYDRATION
CORE
2) Obstructed urethra
CORE
3) could not urinate due to infection
CORE
4) Urinary tract infection
CORE
5) DIARRHEA
CORE
6) IS NOW IN BED, WHERE ALL HIS DAILY NEEDS MUST BE TAKEN CARE OF
CORE
7) LOSS OF MUSCLE TONE
CORE
8) A LOT OF WEAKNESS WHEN WALKING
CORE

3) Drug : Xtandi
Active Substance : 1) ENZALUTAMIDE
Drug Characterization : Suspect
Form of Admin : 1) Capsule
Lot Number : 1) Unknown
Daily Dose : (160 milligram(s), in 1 Day)
Route of Admin : 1) Oral
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Drug withdrawn

Causality

1) DEHYDRATION (Dehydration - 10012174, Dehydration - 10012174)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Obstructed urethra (Urethral obstruction - 10046459, Urethral obstruction - 10046459)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) could not urinate due to infection (Urinary retention - 10046555, Urinary retention - 10046555)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Urinary tract infection (Urinary tract infection - 10046571, Urinary tract infection - 10046571)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) DIARRHEA (Diarrhea - 10012727, Diarrhoea - 10012735)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) IS NOW IN BED, WHERE ALL HIS DAILY NEEDS MUST BE TAKEN CARE OF (Activities of daily living impaired - 10050954, Loss of personal independence in daily activities - 10079487)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) LOSS OF MUSCLE TONE (Hypotonia - 10021118, Hypotonia - 10021118)

Continuation Sheet for CIOMS report

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

8) A LOT OF WEAKNESS WHEN WALKING (Weakness - 10047862, Asthenia - 10003549)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

Drug 3 :XTANDI

1) 160 milligram, qd

23. OTHER RELEVANT HISTORY (Continuation...)

2) BLADDER SURGERY IN ORDER TO BE ABLE TO URINATE (10061699 , Bladder operation)