SUSPECT ADVERSE REACTION REPORT

DO-TOLMAR, INC.-24DO050537

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
JRLP	DOMINICAN Cont..	30	Mar	1926	98	Male			

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

1) Death due to fall (Fall (10016173), Fall (10016173))
(- 02/Jul/2025) - Fatal
2) Death due to hit in the head (Head injury (10019196), Head injury (10019196))
(- 02/Jul/2025) - Fatal
3) Erection problems (Erection failure (10015118), Erectile dysfunction (10061461))
Unknown
4) Urinating problems/patient urinated in small amounts, did not hold back much urine (Reduced bladder capacity (10069645), Reduced bladder capacity (10069645))
Unknown

Cont..

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [x] PATIENT DIED
- [ ] LIFE THREATENING
- [ ] 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) (45 Milligram, Injection)(Unknown)(45 Milligram, Injection) (Unknown)

Cont..

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
1) (45 milligram(s), 1 in 6 Month)	1) Subcutaneous
2) (45 milligram(s), 1 in 6 Month)	2) Subcutaneous

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (14/Apr/2021 -)	

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)

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	DO-TOLMAR, INC.-24DO050537
24c. DATE RECEIVED BY MANUFACTURER: 11/Jul/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 15/Jul/2025	25a. REPORT TYPE: ☐ INITIAL ☑ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

1a. COUNTRY

DOMINICAN REPUBLIC

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

5) The patient begins to feel discomfort because of swelling (Swelling (10042674), Swelling (10042674) - Unknown)

6) High PSA (Prostatic specific antigen increased (10036975), Prostatic specific antigen increased (10036975) - Unknown)

7) Urinated a lot and had to get up, and felt uncomfortable (Pollakiuria (10036018), Pollakiuria (10036018) - Unknown)

Event Description :

This Study report from DOMINICAN REPUBLIC was received by Adium (reference number: DO-ADIUM-DO-0051-20240626) on 26-JUN-2024 from a Consumer regarding an Elderly 98 Years old Male patient who experienced medical significant event of Erection problems (Erection failure) and non-serious events of Urinating problems/patient urinated in small amounts, did not hold back much urine (Reduced bladder capacity), The patient begins to feel discomfort because of swelling (Swelling), High PSA (Prostatic specific antigen increased), urinated a lot and had to get up, and felt uncomfortable (Pollakiuria) 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 27-JUN-2024.

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

Concomitant medications were not reported.

On 14-APR-2021, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration date: not reported). On unknown date, according to information from the patient's urologist, the patient's PSA was high. The patient was currently showing in the laboratory results that were carried out approximately 15 days previous (no values or percentage was available). Since unknown date, the reason that the PSA was high was because the patient had erection problems due to the fact that the patient was 94 or 95 years old (as reported). The patient had prostate problems where nothing more could be done, the prostate cancer must be kept blocked as the patient could not had a biopsy. The date of the next application of the Eligard medication was approaching and the patient began to feel discomfort because of swelling and problems, referring to the fact that the patient urinated in small amounts, did not hold back much urine, urinated a lot and had to get up, and felt uncomfortable. These were the symptoms that the patient had presented when he arrived home, as the reporter was the one who follows up with the medication and took the patient to the doctor, but the patient did not live with the reporter, so the reporter did not know if the patient had only presented these problems, but when the patient took the Eligard medication, he recovered and was calm. On 03-JAN-2024, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration date: not reported). His next application corresponded to JUN-2024. Action taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were not applicable. The outcome of Erection failure was Unknown. The outcome of Reduced bladder capacity was Unknown. The outcome of Swelling was Unknown. The outcome of Prostatic specific antigen increased was Unknown. The outcome of Pollakiuria was Unknown.

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

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

On 11-Jul-2025, follow-up was received from Dominican Republic by Adium (Reference number: DO-ADIUM-DO-0051-20240626 (1)) and sent to Tolmar on 11-Jul-2025. New information included: Added new serious (fatal) events of "Death due to fall" (fall) and "Death due to hit in the head" (head injury), upgraded the seriousness to (Death) and narrative was updated.

On 02-Jul-2025, the patient died due to fall and hit in the head. The patient was 99-year-old at the time of death. It was unknown if an autopsy was performed. No further details were provided.

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

The outcome of the events fall and head injury was fatal.

The reporter assessed the seriousness of the events fall and head injury as serious (death).

The reporter provided the causality of the events fall and head injury as not related in relationship to Eligard and Eligard Unspecified Device.

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

Listedness of previously reported events erectile dysfunction, swelling, prostate specific antigen increased, pollakiuria and reduced bladder capacity were retained as previously assessed

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

Continuation Sheet for CIOMS report

Head injury >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
Head injury> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
Head injury> Eligard®>unlisted as per USPI Eligard®>Feb-2025
Head injury> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding an elderly 98-year-old male patient who experienced erectile dysfunction (Erection problems), reduced bladder capacity, pollakiuria (Urinating problems/patient urinates in small amounts, does not hold back much urine, urinates a lot and has to get up, and feels uncomfortable), swelling (The patient begins to feel discomfort because of swelling) and PSA increased (High PSA) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed the event erectile dysfunction as serious (MS) as it is an IME, while all other events are considered as non-serious as they did not meet ICH seriousness criteria. All the events are considered as not related to Eligard (drug and device) as per the case context they are all attributable to underlying prostate cancer and elderly age of the patient is a strong confounding factor.

FU added events fall (death due to fall) and head injury (death due to hit in head). Tolmar assessed the reported events as serious as it resulted in fatal outcome. The causality of events fall and head injury was assessed as not related to suspect Eligard(drug and device) as fall is accidental in nature and head injury occurred as a consequence of fall which in turn resulted in death of the patient. Elderly age of the patient could be risk factor for the events.

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

Product-Reaction Level

1) Drug	:	Eligard® (Leuprolide acetate)
Active Substance	:	1) Leuprolide acetate
Drug Characterization	:	Suspect
Form Strength	:	1) 45 Milligram
		2) 45 Milligram
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 : 14/Apr/2021 To :Not applicable
		2) From : 03/Jan/2024 To :Not applicable
Action(s) Taken With Drug	:	Not applicable

Causality

1) Death due to fall (Fall - 10016173, Fall - 10016173)

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

2) Death due to hit in the head (Head injury - 10019196, Head injury - 10019196)

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

3) Erection problems (Erection failure - 10015118, Erectile dysfunction - 10061461)

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

4) Urinating problems/patient urinated in small amounts, did not hold back much urine (Reduced bladder capacity - 10069645, Reduced bladder capacity - 10069645)

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

5) The patient begins to feel discomfort because of swelling (Swelling - 10042674, Swelling - 10042674)

Causality as per reporter	:	Not Reported

Continuation Sheet for CIOMS report

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

6) High PSA (Prostatic specific antigen increased - 10036975, Prostatic specific antigen increased - 10036975)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) Urinated a lot and had to get up, and felt uncomfortable (Pollakiuria - 10036018, Pollakiuria - 10036018)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Death due to fall
CORE UnLabeled
2) Death due to hit in the head
CORE UnLabeled
3) Erection problems
CORE Labeled
4) Urinating problems/patient urinated in small amounts, did not hold back much urine
CORE UnLabeled
5) The patient begins to feel discomfort because of swelling
CORE UnLabeled
6) High PSA
CORE Labeled
7) Urinated a lot and had to get up, and felt uncomfortable
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) Unknown
Route of Admin : 1) Subcutaneous
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

1) Death due to fall (Fall - 10016173, Fall - 10016173)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Death due to hit in the head (Head injury - 10019196, Head injury - 10019196)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Erection problems (Erection failure - 10015118, Erectile dysfunction - 10061461)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Urinating problems/patient urinated in small amounts, did not hold back much urine (Reduced bladder capacity - 10069645, Reduced bladder capacity - 10069645)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) The patient begins to feel discomfort because of swelling (Swelling - 10042674, Swelling - 10042674)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) High PSA (Prostatic specific antigen increased - 10036975, Prostatic specific antigen increased - 10036975)

Continuation Sheet for CIOMS report

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

7) Urinated a lot and had to get up, and felt uncomfortable (Pollakiuria - 10036018, Pollakiuria - 10036018)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Death due to fall
CORE
2) Death due to hit in the head
CORE
3) Erection problems
CORE
4) Urinating problems/patient urinated in small amounts, did not hold back much urine
CORE
5) The patient begins to feel discomfort because of swelling
CORE
6) High PSA
CORE
7) Urinated a lot and had to get up, and felt uncomfortable
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

2) 45 milligram, q 6 month