SUSPECT ADVERSE REACTION REPORT

DO-Tolmar-TLM-2025-01602

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
ECT	DOMINICAN Cont..	05	May	1936	89	Male			2025

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

1) Kidney stones (Kidney stones (10023437), Nephrolithiasis (10029148))
(//2025 -) - Not Recovered/Not Resolved/Ongoing
2) vesical balloon (Urinary retention (10046555), Urinary retention (10046555))
(//2025 -) - Not Recovered/Not Resolved/Ongoing
3) Bone metastasis (Metastases to bone (10027452), Metastases to bone (10027452))
Not Recovered/Not Resolved/Ongoing
4) Inguinal hernia (Inguinal hernia (10022016), Inguinal hernia (10022016))
(//2025 -) - Not Recovered/Not Resolved/Ongoing

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) (22.5 Milligram, Injection)(15109CUY; UNK; UNK)(22.5 Milligram, Injection)(Unknown)

Cont..

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

15. DAILY DOSE(S)

1) (22.5 milligram(s), 1 in 3 Month)

2) (22.5 milligram(s), 1 in 3 Month)

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous
2) 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) (/Feb/2024 - 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
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-TLM-2025-01602
24c. DATE RECEIVED BY MANUFACTURER	**24d. REPORT SOURCE**
25/Jun/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	**25a. REPORT TYPE**
02/Jul/2025	☐ 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) Anemia (Anemia (10002272), Anaemia (10002034)(//2025 -) - Recovering/Resolving)

Event Description :

This study report from Dominican Republic was received by Adium via patient support program (Asofarma A Tu Lado) (reference number: DO-ADIUM-DO-0034-20250508) on 08-May-2025, from a consumer (non-healthcare professional) regarding an elderly-89-year-old male patient who experienced serious events of ‘kidney stones' (nephrolithiasis) (medically significant), ‘vesical balloon' (urinary retention) (medically significant) and non-serious events of ‘anemia' (anaemia) and ‘inguinal hernia' (inguinal hernia) during Eligard (leuprolide acetate) 22.5 mg therapy for prostate cancer. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 12-May-2025.

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

Concomitant medications were unknown.

On an unknown date in Feb-2024, the patient began receiving Eligard 22.5 mg every 3 months via subcutaneous route for prostate cancer (Lot numbers: 15109CUY; UNK; UNK expiration dates: May-2026).

On 07-May-2025, the patient received Eligard 22.5 mg every 3 months via subcutaneous route for prostate cancer (Lot numbers and Expiration dates were unknown).

On an unknown date and month in year 2025, the patient had anemia, hemoglobin level of 11g/dl, bladder occlusion due to which he was unable to urinate for which the indwelling urinary catheter was placed, kidney stones which were seen during abdominal ultrasound and an inguinal hernia. No further details were provided.

Corrective treatment included insertion of urinary catheter for urinary retention.

Relevant test results included:

On an unknown date: Haemoglobin: 11g/dl (Ref range: not provided).
On an unknown date: Ultrasound abdomen: kidney stones (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 anaemia was resolving.

The outcome of nephrolithiasis, urinary retention and inguinal hernia was not resolved.

The reporter did not assess the seriousness of nephrolithiasis, urinary retention, anaemia and inguinal hernia.

The reporter assessed the causality of nephrolithiasis, urinary retention, anaemia and inguinal hernia in relation to Eligard and Eligard Unspecified Device as not related.

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

On 25-Jun-2025, follow up from Dominican Republic was received by Adium via Patient Support Program (reference number: DO-ADIUM-DO-0034-20250508) and sent to Tolmar on 26-Jun-2025. New information included: New serious (medically significant) event of "bone metastasis" (metastases to bone) added. Lab test was added.

On an unknown date, the patient underwent scintigraphy which confirmed bone metastasis. No further information reported.

Corrective treatment was not reported.

Relevant test results included:
On an unknown date: Scintigraphy: bone metastasis (Ref. range: Not provided)

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

The outcome of metastases to bone was not resolved.

The reporter did not assess the seriousness of metastases to bone.

The reporter assessed the causality of metastases to bone in relationship to Eligard and Eligard Unspecified Device as not related.

Continuation Sheet for CIOMS report

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

Listedness
Nephrolithiasis>Eligard>Unlisted as per CCDS>07-Nov-2024
Nephrolithiasis>Eligard>Unlisted as per USPI>Feb-2025
Nephrolithiasis>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Nephrolithiasis>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

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

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

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

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding 89-year-old elderly male patient who had nephrolithiasis (kidney stones), urinary retention (vesical balloon), anaemia (anaemia) and inguinal hernia (inguinal hernia) during Eligard (leuprolide acetate) 22.5 mg therapy for prostate cancer. Tolmar assessed the events nephrolithiasis and urinary retention as serious (medically significant) as it is included in IME list and other reported events were assessed as non-serious since they did not meet the ICH seriousness criteria. The reported events were assessed as not related to Eligard (drug and device) considering the inconsistency with the safety profile of the drug, etiology and clinical nature of events. Elderly age and underlying prostate cancer could be confounders.

FU added event of Metastases to bone (bone metastasis). Tolmar assessed the event Metastases to bone as serious as it included in IME list. The causality of event metastases to bone was assessed as not related to suspect Eligard(drug and device) as it could be attributed to underlying prostate cancer which is known to progress despite treatment.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
ABDOMINAL ULTRASOUND			
HAEMOGLOBIN		11 gram per decilitre	
SCINTIGRAPHY			

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

1) Test Name: ABDOMINAL ULTRASOUND

Result Unstructured Data (free text) : Kidney stones

Test Date:

3) Test Name: SCINTIGRAPHY

Result Unstructured Data (free text) : bone metastasis

Test Date:

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

Continuation Sheet for CIOMS report

Product-Reaction Level

1) Drug	:	Eligard® (Leuprolide acetate)
Active Substance	:	1) Leuprolide acetate
Drug Characterization	:	Suspect
Form Strength	:	1) 22.5 Milligram 2) 22.5 Milligram
Form of Admin	:	1) Injection 2) Injection
Lot Number	:	1) 15109CUY; UNK; UNK 2) Unknown
Daily Dose	:	(22.5 milligram(s), 1 in 3 Month) (22.5 milligram(s), 1 in 3 Month)
Route of Admin	:	1) Subcutaneous 2) Subcutaneous
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	1) From : /Feb/2024 To :Continuing 2) From : 07/May/2025 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) Kidney stones (Kidney stones - 10023437, Nephrolithiasis - 10029148)

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

2) vesical balloon (Urinary retention - 10046555, Urinary retention - 10046555)

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

3) Bone metastasis (Metastases to bone - 10027452, Metastases to bone - 10027452)

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

4) Inguinal hernia (Inguinal hernia - 10022016, Inguinal hernia - 10022016)

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

5) Anemia (Anemia - 10002272, Anaemia - 10002034)

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

Labeling :

1) Kidney stones	
CORE	UnLabeled
2) vesical balloon	
CORE	Labeled
3) Bone metastasis	
CORE	Labeled
4) Inguinal hernia	
CORE	UnLabeled
5) Anemia	
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) 15109CUY; UNK; UNK
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]

Continuation Sheet for CIOMS report

Action(s) Taken With Drug : Not applicable

Causality

1) Kidney stones (Kidney stones - 10023437, Nephrolithiasis - 10029148)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) vesical balloon (Urinary retention - 10046555, Urinary retention - 10046555)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Bone metastasis (Metastases to bone - 10027452, Metastases to bone - 10027452)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Inguinal hernia (Inguinal hernia - 10022016, Inguinal hernia - 10022016)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) Anemia (Anemia - 10002272, Anaemia - 10002034)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Kidney stones
CORE
2) vesical balloon
CORE
3) Bone metastasis
CORE
4) Inguinal hernia
CORE
5) Anemia
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 mg

23. OTHER RELEVANT HISTORY (Continuation...)

2) INSERTION OF URINARY CATHETER (10067881 , Urinary catheter insertion) (Continuing : NO)