SUSPECT ADVERSE REACTION REPORT

HN-Tolmar-TLM-2025-00699

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
JMC	HONDURAS	30	Jul	1937	87	Male		Feb	2025

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

1) Retaining urine in his bladder and catheter was placed (Bladder retention (10005071), Urinary retention (10046555)) Unknown
2) Suspension of treatment (Therapy cessation (10065154), Therapy cessation (10065154)) (/Feb/2025 -) - Unknown
3) Eligard was not working for the patient, ineffective drug (Lack of drug effect (10023610), Drug ineffective (10013709)) Unknown

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) (45 Milligram, Injection)(Unknown)(45 Milligram)(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
2) (45 milligram(s), 1 in 6 Month)	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) (//2023 -)	

III. CONCOMITANT DRUG(S) AND HISTORY

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

1)OTHER THERAPEUTIC PRODUCTS(Pressar)(300 Milligram)

Cont..

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

1) PROSTATE CANCER (10060862, Prostate cancer) (//2023 -) (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	HN-Tolmar-TLM-2025-00699
24c. DATE RECEIVED BY MANUFACTURER: 08/Jul/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 11/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...)

Event Description :

This Study report from HONDURAS was received by Adium via Patient Support Program (reference number: HN-ADIUM-HN-0077-20250226) on 26-FEB-2025 from a Consumer/Other Non-Health Prof regarding an Elderly 87 Years old Male patient who experienced a Medically Significant event of Retaining urine in his bladder and catheter was placed (Bladder retention), and a non-serious event of Eligard was not working for the patient, ineffective drug (Lack of drug effect), 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-FEB-2025.

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

Concomitant medications included: PERMIXON.

On an unknown date, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration dates were not reported).

On an unknown date, unknown amount of time after the most recent dose of Eligard, Eligard was not working for the patient (ineffective drug), because it could have come from another quality, as there were several laboratories, and it was not always the same. The patient had presented some irregularities. On an unknown date, unknown amount of time after the most recent dose of Eligard, the patient experienced retaining urine in his bladder. On 20- FEB-2025, the patient received Eligard 45 milligram, q 6 month, via Subcutaneous use (Lot numbers and Expiration dates were not reported). On 21-FEB-2025, the patient had an appointment with the urologist, and they placed a catheter because he was retaining urine. On 22-FEB-2025 the patient underwent Urotac tests and based on the results he might schedule an appointment with the oncologist. Further corrective treatment was not reported. Action taken with Eligard in response to the events was Unknown. De-challenge and re-challenge were Not Applicable. The outcome of Bladder retention was Unknown. The outcome of Lack of drug effect was Unknown.

Relevant test results included:

22-FEB-2025: Urogram: Results not provided

The reporter assessed the event as serious and did not provide a causality of the event in relationship to Eligard.

On 06-MAR-2025, follow-up information was received by Adium Patient support program (reference number: HN-ADIUM-HN-0077-20250226) from a Consumer and a Consumer and sent to Tolmar on 07-MAR-2025. New information included: Additional reporter added as Consumer, added patient information (weight, height), medical history (Blood pressure high), concomitant medication (Pressar, Bicalutamide), product information (approximate Eligard start period), other clinical details.

The patient's medical history included: Blood pressure high.

Concomitant medications included: Pressar and Bicalutamide.

As per reported the patient's weight was approximately 170 (unknown unit) and height was 165 centimeters (cm). On an unspecified date (approximately 3 years ago from the date of this report), the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration dates were not reported). The patient complied with the administration indications, did not consume alcoholic beverages and did not smoke cigarettes. The storage of the drug was refrigerated. On an unknown date, patient went to a doctor's appointment, and indicated that Eligard was not working, so they were currently waiting for his next appointment with the Oncologist on 24-MAR-2025. No further information was reported.

On 11-Apr-2025 Tolmar Quality Assurance completed an evaluation of the technical complaint (QE-026718) and report was sent to Tolmar on 11-Apr-2025. The root cause was inconclusive.

Complaint assessment:

A family member on behalf of a patient reported a unit of Eligard 45mg (lot number not reported) stating that he thinks “Eligard is not working for the patient“and that “there are several laboratories, and it is not always the same”. Follow up received from the family member states “patient went to a doctor's appointment and he indicated that Eligard is not working”. Further information was requested with the administering physician for lot information, date of administration, and lab test values and dates. Follow up has not been received from the physician as of this report; if further information is received, this report will be amended. Per SOP-01003, complaints do not meet the criteria for QCC retain sample testing if a lot number is not reported.

On 16-Dec-2024, Complaint QE-024913 documented the investigation of Eligard 45mg (unknown lot) with the failure mode "medical - lack of effect.” QE-024913 which was closed.

On 26-Feb-2025, the complaint was received. Per SOP-00894, "Any complaint(s) received within 3 months of a previously completed investigation for the same product, lot number and complaint type, may reference the previous investigation." This complaint was received within 3 months of the closure of QE-024913 and therefore will not undergo reinvestigation.

Continuation Sheet for CIOMS report

The conclusion of QE-024913 is as follows: “Without an identified lot number, the executed manufacturing batch records could not be reviewed. However, the drug product must pass strict testing requirements prior to release; manufacturing records, analytical data and other applicable data reviews are performed prior to the release of each lot.
The stability data results for Eligard 45mg supports the product's expiration period. There were no Field Alert Report submissions within the past year related to the reported lack of efficacy. A one-year deviation search did not identify deviations that would have contributed to the reported defect.”

Based on the data review and available information, there is no indication that the root cause of the reported lack of efficacy is related to the manufacturing or packaging process at Tolmar. The investigation of this event did not indicate any impaired quality of the product. Without the lot number, retain sample analysis could not be performed. The root cause is considered inconclusive. Further investigation is not required at this time and this complaint will be included in the system for tracking and trending purposes.

Listedness of events Urinary retention and drug ineffective were retained as per previous assessment.

On 08-Jul-2025, follow-up information from HONDURAS was received by Adium (reference number: HN-ADIUM-HN-0077-20250226(V2)) from a consumer (non-healthcare professional) and sent to Tolmar on 09-Jul-2025. New information included: Updated clinical details of Eligard. Added a new non-serious event of "suspension of treatment" (Therapy cessation) was added.

On an unknown date in 2023, the patient began receiving Eligard 45 mg, every 6 months via subcutaneous route for Prostate cancer (Lot numbers and Expiration dates were not reported).

On an unknown date in Feb-2025, the patient suspended his treatment with the Eligard. No further information was provided.

Corrective treatment was not reported.

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

The outcome of therapy cessation was unknown.

The reporter did not assess the seriousness of therapy cessation.

The reporter assessed the causality of therapy cessation in relationship to Eligard and Eligard Unspecified device as related.

No follow-up queries raised.

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

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding an elderly 87-year-old male patient who experienced urinary retention (Retaining urine in his bladder and catheter was placed) and drug ineffective (Eligard was not working for the patient, ineffective drug) is noted during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed the event urinary retention as serious (MS) as it is an IME event and requires significant intervention to prevent a serious outcome, while drug ineffective is a non-serious event as it did not meet ICH seriousness criteria. Both the events are considered as related to Eligard (drug) based on the inferred temporal relationship and product safety profile. Efficacy of drug varies from person to person and depends on various factors such as pharmacokinetics and pharmacodynamics of the drug. Elderly age and underlying malignancy are considered as risk factors for urinary retention.
In Follow up, added a new non-serious event of therapy cessation (suspension of treatment) was added. The causality for the reported event therapy cessation is assessed as not related with Eligard (drug and device) components as the event had happened due to human decision and action, rather due to the product. Causality of the previous events is retained as per previous assessment.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
UROGRAM	22/Feb/2025		

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

1) Test Name: UROGRAM
Result Unstructured Data (free text) : Urotac tests results not provided
Test Date: 22/Feb/2025

Continuation Sheet for CIOMS report

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
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 : //2023 To :Unknown
2) From : 20/Feb/2025 To :Unknown
Action(s) Taken With Drug : Unknown

Causality

1) Retaining urine in his bladder and catheter was placed (Bladder retention - 10005071, Urinary retention - 10046555)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Suspension of treatment (Therapy cessation - 10065154, Therapy cessation - 10065154)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) Eligard was not working for the patient, ineffective drug (Lack of drug effect - 10023610, Drug ineffective - 10013709)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Retaining urine in his bladder and catheter was placed
CORE Labeled
2) Suspension of treatment
CORE UnLabeled
3) Eligard was not working for the patient, ineffective drug
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
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

1) Retaining urine in his bladder and catheter was placed (Bladder retention - 10005071, Urinary retention - 10046555)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Suspension of treatment (Therapy cessation - 10065154, Therapy cessation - 10065154)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) Eligard was not working for the patient, ineffective drug (Lack of drug effect - 10023610, Drug ineffective - 10013709)

Continuation Sheet for CIOMS report

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

Labeling :

1) Retaining urine in his bladder and catheter was placed
   CORE
2) Suspension of treatment
   CORE
3) Eligard was not working for the patient, ineffective drug
   CORE

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

Dosage Text :

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

1). Drug	:	OTHER THERAPEUTIC PRODUCTS
Active Substance	:	1) Pressar
Form Strength	:	1) 300 Milligram
Daily Dose	:	1) 1200 milligram(s) (300 milligram(s), 1 in 6 Hour)
Route of Admin	:	1) Oral
Indications	:	1) High blood pressure [10020772 - Hypertension]
Dosage Text	:	1) 300 milligram, q 6

2). Drug	:	PERMIXON
Active Substance	:	1) SERENOA REPENS EXTRACT
Form Strength	:	
Indications	:	1) Drug use for unknown indication [10070592 - Product used for unknown indication]

3). Drug	:	BICALUTAMIDE
Active Substance	:	1) BICALUTAMIDE
Form Strength	:	
Daily Dose	:	1) (in 8 Hour)
Route of Admin	:	1) Oral
Indications	:	1) Drug use for unknown indication [10070592 - Product used for unknown indication]
Dosage Text	:	1) UNK, q 8 hr

23. OTHER RELEVANT HISTORY (Continuation...)

2) CATHETER PLACEMENT FOR URINE RETENTION (10052915 , Catheter placement) (21/Feb/2025 -)

3) HIGH BLOOD PRESSURE (10005747 , Blood pressure high)