SUSPECT ADVERSE REACTION REPORT

CR-TOLMAR, INC.-24CR052701

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
PBF	COSTA RICA	15	Sep	1939	85	Male			

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

1) His disease progressed (Disease progression (10061818), Disease progression (10061818))
Not Recovered/Not Resolved/Ongoing
2) CRP and PSA are increasing (C-reactive protein increased (10006825), C-reactive protein increased (10006825))
Not Recovered/Not Resolved/Ongoing
3) Moderate neurological deterioration (Neurological status deterioration (10064098), Neurological decompensation (10068357))
Not Recovered/Not Resolved/Ongoing
4) CRP and PSA are increasing (PSA increased (10037102), Prostatic specific antigen increased (10036975))
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)(Unknown)(22.5 Milligram, Injection)(Unknown)

Cont..

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
1) (22.5 milligram(s), 1 in 3 Month)	1) Subcutaneous
2) (22.5 milligram(s), 1 in 3 Month)	2) Subcutaneous

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

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

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	CR-TOLMAR, INC.-24CR052701
24c. DATE RECEIVED BY MANUFACTURER: 29/Jul/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 01/Aug/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 COSTA RICA was received by Adium (reference number: CR-ADIUM-CR-0548-20240917) via the Patient Support Program "ASOFARMA A TU LADO" on 17-SEP-2024 from a Consumer/Other Non-Health Prof regarding an Elderly 85 Years old Male patient who experienced medically significant serious event of His disease progressed (Disease progression), and non-serious events of CRP and PSA are increasing (C-reactive protein increased and PSA increased), Moderate neurological deterioration (Neurological status deterioration) during Eligard (Leuprolide acetate) 22.5 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 18-SEP-2024.

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

Concomitant medications were not reported.

On 13-OCT-2022, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration dates not provided). On an unspecified date in JUL-2024, the patient received Eligard 22.5 milligram, q 3 month via Subcutaneous use (Lot numbers and Expiration dates not provided). On an unspecified date, unknown amount of time after the most recent dose of Eligard, the patient experienced that that the CRP (C-reactive protein) and PSA (Prostatic specific antigen) were increasing. In addition, he observed a moderate neurological deterioration. On 13-SEP-2024, approximately 2 months after the most recent dose of Eligard, his treating physician suspended the product because his disease progressed. Corrective treatment was not reported. Action taken with Eligard in response to the events was Drug Withdrawn. De-challenge and re-challenge were Unknown. The outcome of Disease progression, C-reactive protein increased, Neurological status deterioration and PSA increased was Not Recovered/Not Resolved.

Relevant test results included:
Unknown date: C-reactive protein: increasing (Ref range: Not provided)
Unknown date: Prostatic specific antigen: increasing (Ref range: Not provided)

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

On 24-Jul-2025, follow-up was received by Adium (Reference number: CR-ADIUM-CR-0548-20240917) via the Patient Support Program "ASOFARMA A TU LADO" from a Consumer (non-healthcare professional) and sent to Tolmar on 25-Jul-2025. New information included: The treatment discontinuation date was updated from "13-Sep-2024" to "unknown".

On an unknown date, the patient's treatment was discontinued but the reporter did not recall the date.

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

Listedness of previously reported events Disease progression, C-reactive protein increased, PSA increased and Neurological status deterioration were retained as previously assessed.

On 29-Jul-2025, follow-up was received by Adium (Reference number: CR-ADIUM-CR-0548-20240917 (2)) via the Patient Support Program "ASOFARMA A TU LADO" from a Consumer (non-healthcare professional) and sent to Tolmar on 30-Jul-2025. New information included: The treatment discontinuation date was updated from "unknown" to "13-Sep-2024". Narrative was updated.

On 13-Sep-2024, the patient's treatment was discontinued, and it was confirmed that Eligard was not resumed thereafter.

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

Company Remarks (Sender's Comments) :

Evaluator Comment (Tolmar): This is regarding an elderly 85-year-old male patient who experienced disease progression (Disease progressed), C-reactive protein increased and PSA increased (CRP and PSA are increasing) and neurological decompensation (Moderate neurological deterioration) during Eligard (Leuprolide acetate) 22.5 mg therapy for prostate cancer. Tolmar assessed the event disease progression as serious (MS) based on its clinical relevance and significant impact on patient's health, while all other events are considered as non-serious as they did not meet ICH seriousness criteria. Events disease progression and PSA increased are attributable to underlying prostate cancer since progression is inherent to it despite treatment. Elderly age is a risk factor for PSA increased. CRP increased is likely due to the concurrent disease progression reported and neurological decompensation is inconsistent with the product safety profile, underlying prostate cancer and elderly age are strong confounders. Hence all the events are considered as not related to Eligard (drug and device).

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value

Continuation Sheet for CIOMS report

CRP	Unknown		
PSA	Unknown		

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

1) Test Name: CRP

Result Unstructured Data (free text) : Increasing.

Test Date: Unknown

2) Test Name: PSA

Result Unstructured Data (free text) : Increasing.

Test Date: Unknown

Lab Comments :

1) Test Name : CRP

Lab Comments : Increasing.

2) Test Name : PSA

Lab Comments : Increasing.

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

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) Unknown
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 : 13/Oct/2022 To :
2) From : /Jul/2024 To :13/Sep/2024
Action(s) Taken With Drug : Drug withdrawn

Causality

1) His disease progressed (Disease progression - 10061818, Disease progression - 10061818)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Unknown
ReChallenge : Unknown

2) CRP and PSA are increasing (C-reactive protein increased - 10006825, C-reactive protein increased - 10006825)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Unknown
ReChallenge : Unknown

3) Moderate neurological deterioration (Neurological status deterioration - 10064098, Neurological decompensation - 10068357)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Unknown
ReChallenge : Unknown

4) CRP and PSA are increasing (PSA increased - 10037102, Prostatic specific antigen increased - 10036975)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Unknown
ReChallenge : Unknown

Continuation Sheet for CIOMS report

Labeling :

1) His disease progressed
CORE Labeled
2) CRP and PSA are increasing
CORE UnLabeled
3) Moderate neurological deterioration
CORE UnLabeled
4) CRP and PSA are increasing
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) His disease progressed (Disease progression - 10061818, Disease progression - 10061818)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) CRP and PSA are increasing (C-reactive protein increased - 10006825, C-reactive protein increased - 10006825)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) Moderate neurological deterioration (Neurological status deterioration - 10064098, Neurological decompensation - 10068357)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) CRP and PSA are increasing (PSA increased - 10037102, Prostatic specific antigen increased - 10036975)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) His disease progressed
CORE
2) CRP and PSA are increasing
CORE
3) Moderate neurological deterioration
CORE
4) CRP and PSA are increasing
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 milligram, q 3 month

2) 22.5 milligram, q 3 month

Drug 2 :Eligard® Unspecified Device

1) UNK