SUSPECT ADVERSE REACTION REPORT

PA-TOLMAR, INC.-24PA051215

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
R-H	PANAMA	29	Mar	1937	87	Male			2021

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

1) Patient died in early April (Death (10011906), Death (10011906))
(- /Apr/2025) - Fatal
2) ENDOCARDITIS/HEART PROBLEMS (Endocarditis (10014665), Endocarditis (10014665))
(/Jun/2024 -) - Not Recovered/Not Resolved/Ongoing
3) RENAL DISEASE/PATIENT HAS PROBLEMS IN BOTH KIDNEYS (Renal disease (10051051), Nephropathy (10029151))
(//2021 -) - Unknown
4) THE NEXT APPLICATION THAT WAS DUE IN JUNE, HAD RECEIVED A CALL TO INDICATE THAT IT WAS DUE IN JUNE, BUT IT WAS NOT APPLIED BECAUSE THEY NEVER WENT TO APPLY IT TO THE PATIENT/ IN THE MONTH OF JULY 2024 WAS TOLD THAT ELIGARD WAS GOING TO BE APPLIED, BU (Intentional dose omission (10079221), Intentional dose omission (10079221))
(//2024 -) - Unknown

Cont..

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [x] PATIENT DIED
- [ ] LIFE THREATENING
- [x] 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) (Injection)(Unknown)(Unknown)(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
(23-Jul-2024 - //2025)	

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) (Asked but Unknown -) (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.-24PA051215
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
22/Apr/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
03/May/2025	☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) PATIENT WAS DUE TO RECEIVE ELIGARD IN JANUARY 2025, BUT IT HAS NOT YET BEEN APPLIED, BECAUSE SINCE 16 DECEMBER 2024

THE PATIENT HAS BEEN HOSPITALISED (Intentional dose omission (10079221), Intentional dose omission (10079221)(/Jan/2025 -) - Unknown)

Event Description :

This Study report from PANAMA was received by Adium via Patient Support Program (reference number: PA-ADIUM-PA-0044-20240722) on 22-JUL-2024 from a Consumer/Other Non-Health Prof regarding an Elderly 87 Years old Male patient who experienced serious (Hospitalization) event of Endocarditis (Endocarditis), the next application that was due in June, had received a call to indicate that it was due in June, but it was not applied because they never went to apply it to the patient/ in the month of July 2024 was told that Eligard was going to be applied, but the patient was already hospitalized (Intentional dose omission), 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 22-JUL-2024.

The patient's medical history and current conditions included Prostate cancer, Dialysis. The reporter stated that the patient had been suffering from prostate cancer for many years, the reporter could only provide information of the 2 years that the patient had been living with the reporter.

Concomitant medications were not reported.

On 21-SEP-2021, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Lot number details not provided). On an unspecified date in 2021 (reported as for 3 years), the patient was diagnosed with renal disease and for this reason he was receiving dialysis 3 times a week. In JAN-2024, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (Lot number details not provided) and it was reported to be the last Eligard application the patient had. The next Eligard application was due in JUN-2024, but it was not applied because they never went to apply it to the patient. It was also reported that the patient was due to receive Eligard in JUL-2024 and when the nurse called to coordinate the application of the medication, the patient was hospitalized due to Endocarditis, in Jun 2024. On 18-JUL-2024, after 3 weeks of hospitalization, the patient was discharged from the hospital. Corrective treatment included unspecified medication. Action taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were not applicable. The outcome of Endocarditis was Unknown. The outcome of renal disease was Unknown. The outcome of Intentional dose omission was Unknown.

The reporter assessed the seriousness of Endocarditis as serious (Hospitalization) and did not assess the causality in relationship to Eligard. The reporter did not assess the seriousness and the causality in relationship to Eligard for the remaining events.

On 15-JAN-2025, follow-up information was received by Adium via ASOFARMA A TU LADO patient support program (reference number: PA-ADIUM-PA-0044-20240722) from a Patient Family Member and sent to Tolmar on 16-JAN-2025. New information included: Added new non-serious event of "patient was due to receive Eligard in January 2025, but it has not yet been applied, because since 16 December 2024 the patient has been hospitalized" (Intentional dose omission), added the most recent dose of Eligard, treatment medications as other therapeutic products, lab data, outcome of event Endocarditis was updated from Unknown to Not Recovered/Not Resolved and clinical details of event Endocarditis as "heart problems" and clinical details of event renal disease.

Since an unspecified date in 2021, unknown time after the most recent dose of Eligard, the patient has problems in both kidneys and for this reason dialysis was performed three times a week. The patient had taken many medicines (unspecified names). On 23-JUL-2024, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (Lot number and expiration date were not reported). On 16-DEC-2024, 4 months 24 days after the most recent dose of Eligard, the patient had been hospitalized for heart problems. The patient was due to receive Eligard in JAN-2025, but it had not been applied, because he was hospitalized. Corrective treatments for Endocarditis and renal disease included unspecified medication. Action taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were not applicable. The outcome of Endocarditis was Not Recovered/Not Resolved. The outcome of renal disease was Unknown. The outcome of Intentional dose omission was Unknown.

Relevant test results included:
On an unknown date: Laboratory test (unspecified name): Unknown results (No units or values provided).

The reporter assessed the seriousness of Endocarditis as serious (Hospitalization). The reporter did not assess the causality of events endocarditis, renal disease, intentional dose omission in relationship to Eligard.

FU added event of Intentional dose omission (the patient was due to receive Eligard in JAN-2025, but it had not been applied, because he was hospitalized). Tolmar assessed Intentional dose omission as non-serious since it did not meet ICH seriousness criteria and as not related to Eligard (drug and device) as it was attributable to human action.

On 22-Apr-2025, follow-up information from Panama was received by Adium via ‘ASOFARMA A TU LADO' Patient Support Program (reference number: PA-ADIUM-PA-0044-20240722) via Patients Support Program from a consumer (patient family member) and sent to Tolmar on 23-Apr-2025. New information included: Added a new serious event of ‘patient died in early April'' (death).

On an unknown date in early Apr-2025, the patient died. The patient was 88-year-old at the time of his death. It was unclear whether an autopsy was performed, and the cause of death remained unknown. No further details were available.

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

The outcome of death was fatal.

Continuation Sheet for CIOMS report

The reporter assessed the seriousness of death as serious (death).

The reporter did not provide the causality of death in relationship to Eligard and Eligard unspecified device.

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

Listedness:

Listedness of events endocarditis, nephropathy and intentional dose omission was retained as per previous assessment.

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

Company Remarks (Sender's Comments) :

Evaluator Comment (Tolmar): This 87 years old male patient had Endocarditis (Endocarditis), Nephropathy (Renal disease), and Intentional dose omission (the next application that was due in June, had received a call to indicate that it was due in June, but it was not applied because they never went to apply it to the patient/ in the month of July 2024 was told that Eligard was going to be applied, but the patient was already hospitalized) during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. Tolmar maintained seriousness of the event Endocarditis as hospitalization; Nephropathy was assessed as medically significant based on its nature and intervention with dialysis and the remaining events as non-serious since they did not meet ICH seriousness criteria. All events were assessed as not related to Eligard (drug and device) based on the etio-pathology of the events, known safety profile of the drug and inconsistency with drug properties. Intentional dose omission was due to human action.
FU added event of Intentional dose omission (the patient was due to receive Eligard in JAN-2025, but it had not been applied, because he was hospitalized). Tolmar assessed Intentional dose omission as non-serious since it did not meet ICH seriousness criteria and as not related to Eligard (drug and device) as it was attributable to human action.
FU added fatal event of death (Patient died in early April). Tolmar assessed death as serious due to fatal outcome. Causal role of Eligard (drug component) in the patient's death was not assessable as lack of information regarding cause of death, events or circumstances preceding patient's death, autopsy report, relevant medical history, supportive investigations that could indicate cause of death, concomitant medications received by the patient precludes meaningful medical assessment of the report. However, advanced age of the patient, underlying prostate cancer, patient having nephropathy and endocarditis were pre-existing risk factors for the patient's death. Death was assessed as not related to the device component of Eligard.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
LABORATORY TEST	Unknown		

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

1) Test Name: LABORATORY TEST

Result Unstructured Data (free text) : Unknown results (No units or values provided).

Test Date: Unknown

Lab Comments :

1) Test Name : LABORATORY TEST

Lab Comments : Unknown results (No units or values provided).

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
2) Injection
3) Injection
Lot Number : 1) Unknown
2) Unknown
3) Unknown

Continuation Sheet for CIOMS report

Daily Dose	:	(45 milligram(s), 1 in 6 Month) (45 milligram(s), 1 in 6 Month) (45 milligram(s), 1 in 6 Month)
Route of Admin	:	1) Subcutaneous 2) Subcutaneous 3) Subcutaneous
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	1) From : To ://2025 2) From : 21/Sep/2021 To :Not applicable 3) From : /Jan/2024 To :Not applicable
Action(s) Taken With Drug	:	Not applicable

Causality

1) Patient died in early April (Death - 10011906, Death - 10011906)

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

2) ENDOCARDITIS/HEART PROBLEMS (Endocarditis - 10014665, Endocarditis - 10014665)

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

3) RENAL DISEASE/PATIENT HAS PROBLEMS IN BOTH KIDNEYS (Renal disease - 10051051, Nephropathy - 10029151)

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

4) THE NEXT APPLICATION THAT WAS DUE IN JUNE, HAD RECEIVED A CALL TO INDICATE THAT IT WAS DUE IN JUNE, BUT IT WAS NOT APPLIED BECAUSE THEY NEVER WENT TO APPLY IT TO THE PATIENT/ IN THE MONTH OF JULY 2024 WAS TOLD THAT ELIGARD WAS GOING TO BE APPLIED, BU (Intentional dose omission - 10079221, Intentional dose omission - 10079221)

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

5) PATIENT WAS DUE TO RECEIVE ELIGARD IN JANUARY 2025, BUT IT HAS NOT YET BEEN APPLIED, BECAUSE SINCE 16 DECEMBER 2024 THE PATIENT HAS BEEN HOSPITALISED (Intentional dose omission - 10079221, Intentional dose omission - 10079221)

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

Labeling :

1) Patient died in early April
CORE UnLabeled

2) ENDOCARDITIS/HEART PROBLEMS
CORE UnLabeled

3) RENAL DISEASE/PATIENT HAS PROBLEMS IN BOTH KIDNEYS
CORE UnLabeled

4) THE NEXT APPLICATION THAT WAS DUE IN JUNE, HAD RECEIVED A CALL TO INDICATE THAT IT WAS DUE IN JUNE, BUT IT WAS NOT APPLIED BECAUSE THEY NEVER WENT TO APPLY IT TO THE PATIENT/ IN THE MONTH OF JULY 2024 WAS TOLD THAT ELIGARD WAS GOING TO BE APPLIED, BU
CORE UnLabeled

5) PATIENT WAS DUE TO RECEIVE ELIGARD IN JANUARY 2025, BUT IT HAS NOT YET BEEN APPLIED, BECAUSE SINCE 16 DECEMBER 2024 THE PATIENT HAS BEEN HOSPITALISED
CORE UnLabeled

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

Causality

1) Patient died in early April (Death - 10011906, Death - 10011906)

Continuation Sheet for CIOMS report

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

2) ENDOCARDITIS/HEART PROBLEMS (Endocarditis - 10014665, Endocarditis - 10014665)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) RENAL DISEASE/PATIENT HAS PROBLEMS IN BOTH KIDNEYS (Renal disease - 10051051, Nephropathy - 10029151)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) THE NEXT APPLICATION THAT WAS DUE IN JUNE, HAD RECEIVED A CALL TO INDICATE THAT IT WAS DUE IN JUNE, BUT IT WAS NOT APPLIED BECAUSE THEY NEVER WENT TO APPLY IT TO THE PATIENT/ IN THE MONTH OF JULY 2024 WAS TOLD THAT ELIGARD WAS GOING TO BE APPLIED, BU (Intentional dose omission - 10079221, Intentional dose omission - 10079221)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) PATIENT WAS DUE TO RECEIVE ELIGARD IN JANUARY 2025, BUT IT HAS NOT YET BEEN APPLIED, BECAUSE SINCE 16 DECEMBER 2024 THE PATIENT HAS BEEN HOSPITALISED (Intentional dose omission - 10079221, Intentional dose omission - 10079221)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Patient died in early April
CORE
2) ENDOCARDITIS/HEART PROBLEMS
CORE
3) RENAL DISEASE/PATIENT HAS PROBLEMS IN BOTH KIDNEYS
CORE
4) THE NEXT APPLICATION THAT WAS DUE IN JUNE, HAD RECEIVED A CALL TO INDICATE THAT IT WAS DUE IN JUNE, BUT IT WAS NOT APPLIED BECAUSE THEY NEVER WENT TO APPLY IT TO THE PATIENT/ IN THE MONTH OF JULY 2024 WAS TOLD THAT ELIGARD WAS GOING TO BE APPLIED, BU
CORE
5) PATIENT WAS DUE TO RECEIVE ELIGARD IN JANUARY 2025, BUT IT HAS NOT YET BEEN APPLIED, BECAUSE SINCE 16 DECEMBER 2024 THE PATIENT HAS BEEN HOSPITALISED
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

2) 45 milligram, q 6 month

3) 45 milligram, q 6 month

23. OTHER RELEVANT HISTORY (Continuation...)

2) DIALYSIS (10061105 , Dialysis) (Continuing : NO)