CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

TLM-2025-03227; PA-TOLMAR, INC.-25PA055514

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	4-6 REACTION ONSET		
		Day	Month	Year	Years		Day	Month	Year
R-M	PANAMA	24	Jun	1940	84	Male			2023

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

1) Generalized deterioration (General physical health deterioration (10049438), General physical health deterioration (10049438))
(/May/2025 - 06/Jun/2025) - Fatal
2) PATIENT CAN NO LONGER EAT THINGS (SOLIDS) (Feeding disorder (10061148), Feeding disorder (10061148))
(//2023 -) - Not Recovered/Not Resolved/Ongoing
3) NO LONGER EAT THINGS (SOLIDS) BECAUSE OTHERWISE HE CHOKES (Choking (10008589), Choking (10008589))
(//2023 -) - Unknown
4) HAD A HEART PROBLEM (Heart disorder (10019277), Cardiac disorder (10061024))
(//2024 -) - Unknown

Cont..

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [x] PATIENT DIED
- [x] LIFE THREATENING
- [x] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [x] 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)

Cont..

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

15. DAILY DOSE(S)

1) (45 milligram(s), 1 in 6 Month)
2) (45 milligram(s), 1 in 6 Month)

Cont..

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous
2) Subcutaneous

Cont..

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ NA

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Prostate Cancer [10060862 - Prostate cancer]

Cont..

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
(09-Mar-2023 -)	

III. CONCOMITANT DRUG(S) AND HISTORY

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

1)PLATELETS(PLATELETS, HUMAN BLOOD)(Tablet)

Cont..

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

1) THROMBOSIS IN BOTH LEGS (10043623, Thrombosis leg) (//2015 -) (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	TLM-2025-03227; PA-TOLMAR,
24c. DATE RECEIVED BY MANUFACTURER	**24d. REPORT SOURCE**
05/Jun/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	**25a. REPORT TYPE**
16/Jun/2025	☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) THYROID PROBLEMS (Thyroid disorder (10043709), Thyroid disorder (10043709) - Not Recovered/Not Resolved/Ongoing)

6) APPLICATIONS OF ELIGARD FOR THE PATIENT WERE PAINFUL (Pain injection site (10033453), Injection site pain (10022086) - Unknown)

Event Description :

This Study report from PANAMA was received by Adium (reference number: PA-0079-20220827) on 06-JAN-2025 from a Consumer/Other Non-Health Prof (patient and patient's wife) regarding an Elderly 84 Years old Male patient who experienced serious (Disability) event Patient can no longer eat things (solids) (Feeding disorder), medically Significant event of no longer eat things (solids) because otherwise he chokes (Choking) and non-serious events of Thyroid problems (Thyroid disorder), Had a heart problem (Heart disorder), during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. The needle component of the constituent device was not identified in the report. Xtandi (enzalutamide) was also considered as suspect. The report was sent to Tolmar on 07-JAN-2025.

The patient's medical history and current conditions included Prostate cancer, Diabetes mellitus, Dementia Alzheimer's type, Epilepsy, Thrombosis, Prostatic operation, Thrombectomy, Osteoporosis, Gastrointestinal tube insertion, Gait inability, Bedridden.

Concomitant medications included platelets, warfarin, phenobarbital and Latradecto and Cepraval.

On 09-MAR-2023, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Lot numbers: unknown; Expiration date: unknown). On an unspecified date in 2023, unknown time after most recent dose of Eligard, the patient was unable to eat alone and could only eat crushed medications and food because the patient no longer ate solids otherwise, he chocked. On an unspecified date, at unknown time from most recent dose of Eligard, the patient experienced thyroid problems for which he took medications (names not specified). On an unspecified date in 2024, unknown time after most recent dose of Eligard, the patient experienced a heart problem. The patient had heart murmur, and the tube was placed so the patient was able to eat, later they took the tube out and since then the patient can no longer eat normal food, but everything must be soft. The patient's wife did not know when the last application of Eligard was because the nurse who arrived was the one who knew the information and did not have her details. The patient's wife believed that, in the month of DEC-2024, it was the patient's turn to receive Eligard, but she had not yet been called (to give her a date). She mentioned that the patient only continued with Xtandi.

Corrective treatment was not reported for event Heart disorder.

Action taken with Eligard in response to the events was drug withdrawn. De-challenge was Unknown, and re-challenge was Unknown.

Action taken with XTANDI in response to the events was dose not changed. De-challenge was Unknown, and re-challenge was Unknown.

The outcome of Feeding disorder was Not Recovered/Not Resolved. The outcome of Choking was Unknown. The outcome of Thyroid disorder was Not Recovered/Not Resolved. The outcome of Heart disorder was Unknown.

Relevant test results included:
Unknown date: Cardiac murmur: Result not provided (Ref range: Not provided).

The reporters assess the seriousness of the event feeding disorder as serious (Disability) and did not assess the seriousness of the events Choking, Thyroid disorder and Heart disorder. The reporters did not assess the causality of the events in relationship to Eligard.

On 21-JAN-2025, follow-up information was received by Adium (reference number: PA-0079-20220827) from a Consumer/Other Non-Health Prof (patient's wife) and sent to Tolmar on 22-JAN-2025. New information included non-serious event of applications of Eligard for the patient were painful (Pain injection site), Eligard details, action taken and narrative were updated.

On an unknown date in 2024, the patient received last Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration dates were Not provided). On an unspecified date, unknown time after the most recent dose of Eligard, the patient no longer continued to apply Eligard as indicated by the physician, who stated that it was no longer necessary. On an unspecified date, unknown time after the most recent dose of Eligard, the patient experienced that applications of Eligard were painful for the patient because he was already advanced in age. However, in relation to Xtandi, it worked well for him.

Action taken with Eligard in response to the events was Drug withdrawn. De-challenge was Not applicable, and re-challenge was Not applicable.

The outcome of Pain injection site was Unknown.

The reporters did not assess the seriousness and causality of the event in relationship to Eligard.

On 05-Jun-2025, follow up information was received via by Adium ((reference number: (PA-0079-20220827 (6)) from a consumer (patient's family member) (non-healthcare professional) New information included: New serious event of ‘generalized deterioration' (general physical health deterioration) was added. The report was sent to Tolmar on 06-Jun-2025.

On an unknown date, in May-2025 the patient was hospitalized for 15 days, and his condition was critical. No further details were provided.

Further corrective treatment was unknown.

Continuation Sheet for CIOMS report

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

The outcome of general physical health deterioration was not resolved.

The reporter assessed the seriousness of event general physical health deterioration as serious (hospitalization and life threatening).

The reporter did not provide the causality for general physical health deterioration in relationship to Eligard and Eligard Unspecified Device.

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

On 06-Jun-2025, follow up information was received via by Adium ((reference number: (PA-0079-20220827 (7)) from a consumer (patient's wife) (non-healthcare professional). New information included: The outcome of event general physical health deterioration was updated from ‘not resolved' to ‘fatal'. Death details were added. Action taken was updated from ‘drug withdrawn' to ‘not applicable'. The report was sent to Tomar on 09-Jun-2025.

On 06-Jun-2025, the patient's wife reported passed away at night due to generalized deterioration. Additionally, the patient's wife mentioned that the patient's health condition became complicated due to diabetes and cancer. The patient was 84-year-old at the time of his death. It was unknown if an autopsy was performed. No further details were provided.

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

The outcome of general physical health deterioration was fatal.

The reporter assesses the seriousness of event general physical health deterioration as serious (death).

The reporter did not provide the causality for general physical health deterioration in relationship to Eligard and Eligard Unspecified Device.

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

On 11-Jun-2025, follow up information was received via by Adium ((reference number: (PA-0079-20220827 (8)) from a consumer (non-healthcare professional) and the report was sent to Tolmar on 12-Jun-2025. No new information was added. Hence, this follow up was considered as non-significant.

No follow up queries were raised.

Listedness of previously reported events feeding disorder, choking, thyroid disorder, cardiac disorder and injection site pain were retained as previously assessed.

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

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding an elderly 84-year-old male patient who experienced feeding disorder (Patient can no longer eat things (solids), choking (no longer eat things (solids) because otherwise he chokes), thyroid disorder (Thyroid problems) and cardiac disorder (Had a heart problem) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar retained the event feeding disorder as serious (disability as reported, choking is considered as serious (MS) based on the clinical relevance of event and is an IME event, while all other events are non-serious as they did not meet ICH seriousness criteria. All the events are considered as not related to Eligard (drug and device). Feeding disorder is likely due to elderly age and impact of underlying malignancy and medical conditions of the patient, choking is due to intake to solid foods as reported. Information regarding thyroid disorder and cardiac disorder are limited and inconsistent with the product safety profile and they are attributable to medical history of the patient.
Based on the follow up information reported patient experienced injection site pain (applications of Eligard for the patient were painful). Tolmar assessed the event as non-serious as it did not meet ICH seriousness criteria. Event is considered as related to Eligard (drug and device) based on the temporal relationship and consistency of the event with product safety profile.

FU added event general physical health deterioration (Generalized deterioration). Tolmar assessed the event general physical health deterioration as serious due to fatal outcome, life-threatening and led to hospitalisation. The causality of event general physical health deterioration was assessed as not related to suspect Eligard(drug and device) considering the nature of event, inconsistency with the safety profile of the drug. Underlying prostate cancer and comorbid condition like diabetes could be confounding factor for the events. Noncompany suspect could be confounder in the case.

Additional Information (Continuation...)

Lab Result :

Continuation Sheet for CIOMS report

Test Name	Test Date	Test Result	Normal Value
HEART MURMUR	Unknown		

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

1) Test Name: HEART MURMUR

Result Unstructured Data (free text) : Result not provided

Test Date: Unknown

Lab Comments :

1) Test Name : HEART MURMUR

Lab Comments : Result not provided

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
Form of Admin : 1) Injection
2) Injection
Lot Number : 1) 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 : 2) From : //2024 To :
Action(s) Taken With Drug : Not applicable

Causality

1) Generalized deterioration (General physical health deterioration - 10049438, General physical health deterioration - 10049438)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) PATIENT CAN NO LONGER EAT THINGS (SOLIDS) (Feeding disorder - 10061148, Feeding disorder - 10061148)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) NO LONGER EAT THINGS (SOLIDS) BECAUSE OTHERWISE HE CHOKES (Choking - 10008589, Choking - 10008589)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) HAD A HEART PROBLEM (Heart disorder - 10019277, Cardiac disorder - 10061024)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) THYROID PROBLEMS (Thyroid disorder - 10043709, Thyroid disorder - 10043709)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) APPLICATIONS OF ELIGARD FOR THE PATIENT WERE PAINFUL (Pain injection site - 10033453, Injection site pain - 10022086)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Continuation Sheet for CIOMS report

Labeling :

1) Generalized deterioration
CORE UnLabeled
2) PATIENT CAN NO LONGER EAT THINGS (SOLIDS)
CORE UnLabeled
3) NO LONGER EAT THINGS (SOLIDS) BECAUSE OTHERWISE HE CHOKES
CORE UnLabeled
4) HAD A HEART PROBLEM
CORE UnLabeled
5) THYROID PROBLEMS
CORE UnLabeled
6) APPLICATIONS OF ELIGARD FOR THE PATIENT WERE PAINFUL
CORE Labeled

2) Drug : Eligard® Unspecified Device (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
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) Generalized deterioration (General physical health deterioration - 10049438, General physical health deterioration - 10049438)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) PATIENT CAN NO LONGER EAT THINGS (SOLIDS) (Feeding disorder - 10061148, Feeding disorder - 10061148)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) NO LONGER EAT THINGS (SOLIDS) BECAUSE OTHERWISE HE CHOKES (Choking - 10008589, Choking - 10008589)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) HAD A HEART PROBLEM (Heart disorder - 10019277, Cardiac disorder - 10061024)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
5) THYROID PROBLEMS (Thyroid disorder - 10043709, Thyroid disorder - 10043709)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
6) APPLICATIONS OF ELIGARD FOR THE PATIENT WERE PAINFUL (Pain injection site - 10033453, Injection site pain - 10022086)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Generalized deterioration
CORE
2) PATIENT CAN NO LONGER EAT THINGS (SOLIDS)
CORE
3) NO LONGER EAT THINGS (SOLIDS) BECAUSE OTHERWISE HE CHOKES
CORE
4) HAD A HEART PROBLEM
CORE
5) THYROID PROBLEMS
CORE
6) APPLICATIONS OF ELIGARD FOR THE PATIENT WERE PAINFUL

Continuation Sheet for CIOMS report

CORE

3) Drug : XTANDI
Active Substance : 1) ENZALUTAMIDE
Drug Characterization : Suspect
Form of Admin : 1) Capsule
2) Capsule
Lot Number : 1) Unknown
2) Unknown
Daily Dose : 1) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)
2) 4.0 dosage form (4 dosage form, 1 in 1 Day)
Route of Admin : 1) Oral
2) Oral
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates : 1) From : 28/Jan/2019 To :Not applicable
2) From : 28/Jan/2019 To :Not applicable
Action(s) Taken With Drug : Not applicable

Causality

1) Generalized deterioration (General physical health deterioration - 10049438, General physical health deterioration - 10049438)
Causality as per reporter : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) PATIENT CAN NO LONGER EAT THINGS (SOLIDS) (Feeding disorder - 10061148, Feeding disorder - 10061148)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) NO LONGER EAT THINGS (SOLIDS) BECAUSE OTHERWISE HE CHOKES (Choking - 10008589, Choking - 10008589)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) HAD A HEART PROBLEM (Heart disorder - 10019277, Cardiac disorder - 10061024)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable
5) THYROID PROBLEMS (Thyroid disorder - 10043709, Thyroid disorder - 10043709)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable
6) APPLICATIONS OF ELIGARD FOR THE PATIENT WERE PAINFUL (Pain injection site - 10033453, Injection site pain - 10022086)
Causality as per reporter : Not Reported
DeChallenge : Not applicable
ReChallenge : Not Applicable

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

2) 45 milligram, q 6 month

Drug 2 :Eligard® Unspecified Device

1) UNK

Drug 3 :XTANDI

1) 160 milligram, qd

2) 4 dosage form (capsules), qd

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

1). Drug : PLATELETS
Active Substance : 1) PLATELETS, HUMAN BLOOD
Form Strength :
Form of Admin : 1) Tablet

Continuation Sheet for CIOMS report

Daily Dose	:	1) (1000 milligram(s))
Route of Admin	:	1) Oral
Indications	:	1) Epilepsy [10015037 - Epilepsy]
Dosage Text	:	1) 1000 milligram 1 at night and half a tablet in the morning

2). Drug	:	WARFARIN
Active Substance	:	1) WARFARIN
Form Strength	:	
Indications	:	1) Thrombosis [10043607 - Thrombosis]

3). Drug	:	PHENOBARBITAL
Active Substance	:	1) PHENOBARBITAL
Form Strength	:	
Daily Dose	:	1) 128 milligram(s) (64 milligram(s), 2 in 1 Day)
Indications	:	1) Drug use for unknown indication [10057097 - Drug use for unknown indication]
Dosage Text	:	1) 64 milligram, bid

4). Drug	:	Latradecto
Active Substance	:	1) Latradecto
Form Strength	:	
Indications	:	1) Thrombosis [10043607 - Thrombosis]
Dosage Text	:	1) Discontinued

5). Drug	:	Cepraval
Active Substance	:	1) Cepraval
Form Strength	:	
Indications	:	1) Drug use for unknown indication [10057097 - Drug use for unknown indication]

23. OTHER RELEVANT HISTORY (Continuation...)

2) ALZHEIMER (10012271 , Dementia Alzheimer's type) (//2020 -) (Continuing : YES)

3) EPILEPTIC SEIZURE (10015052 , Epileptic seizure) (//2020 -) (Continuing : YES)

4) PROSTATE CANCER (10060862 , Prostate cancer) (Asked but Unknown -) (Continuing : YES)

5) DIABETES (10012594 , Diabetes) (Asked but Unknown -) (Continuing : YES)

6) OPERATED FOR PROSTATE CANCER (10048605 , Prostatic operation NOS) (Asked but Unknown -) (Continuing : NO)

7) OPERATED ON THE LEFT LEG PLACING A MESH SO THAT THE CLOT DOES NOT GO TO THE LUNGS AND HEART (10043530 , Thrombectomy) (Asked but Unknown -) (Continuing : NO)

8) OSTEOPOROSIS (10031282 , Osteoporosis) (Asked but Unknown -) (Continuing : YES)

9) THEY PUT A TUBE IN THE PATIENT SO HE COULD EAT (10051041 , Feeding tube insertion) (Asked but Unknown - Asked but Unknown) (Continuing : NO)

10) UNABLE TO WALK (10049278 , Unable to walk) (Asked but Unknown -) (Continuing : YES)

11) BEDRIDDEN (10048948 , Bedridden) (Asked but Unknown -) (Continuing : YES)