SUSPECT ADVERSE REACTION REPORT

PA-Tolmar-TLM-2025-03884

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
T-F	PANAMA	13	Nov	1946	78	Male		May	2025

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

1) heart failure (Heart failure (10019279), Cardiac failure (10007554))
Not Recovered/Not Resolved/Ongoing
2) Lower Extremity Edema (Lower leg edema (10078347), Oedema peripheral (10030124))
(/May/2025 -) - Recovering/Resolving
3) obstruction of the veins by fat (Arteriosclerosis (10003210), Arteriosclerosis (10003210))
Unknown

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) (Injection)(Unknown)

Cont..

15. DAILY DOSE(S)

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

Cont..

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous

Cont..

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

Cont..

18. THERAPY DATE(S) (from/to)

1) (10/May/2022 - ongoing)

19. THERAPY DURATION

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 ☐ YES ☐ NO

24b. MFR CONTROL NO.

PA-Tolmar-TLM-2025-03884

24c. DATE RECEIVED BY MANUFACTURER

19/Jun/2025

24d. REPORT SOURCE ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL

DATE OF THIS REPORT

26/Jun/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 Panama was received by Adium via Patient Support Program (reference no. PA-ADIUM-PA-0067-20250619 (0)) on 19-Jun-2025 from a consumer (other healthcare professional) regarding an elderly 78-year-old male patient who experienced serious events of 'heart failure' (cardiac failure) (life threatening) (medically significant) (permanent disability) and 'Lower Extremity Edema' (Oedema peripheral) (permanent disability) and a non-serious event of 'obstruction of the veins by fat' (Arteriosclerosis) during Eligard (leuprolide acetate) 45 mg therapy for prostate cancer. The needle component of the constituent device was not identified in the report. Xtandi (enzalutamide) was also considered as a suspect. The report was sent to Tolmar on 20-Jun-2025.

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

Concomitant medications were unknown.

On 10-May-2022, the patient began receiving Eligard 45 mg, every 6 months, via subcutaneous route for prostate cancer (Lot number and Expiration date were not reported).

On an unknown date, the patient experienced heart failure and obstruction of the veins by fat.

On an unknown date in May-2025, the patient experienced significant edema in his lower limbs which had been related to his heart failure which was likely caused by vein obstruction due to fat deposits. As a result, walking has become difficult for him due to swelling in legs and feet. No further information was provided.

Corrective treatment included enalapril for heart failure and unspecified topical creams and antibiotics for his lower extremity edema.

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

The outcome of cardiac failure was not recovered, oedema peripheral was recovering, and arteriosclerosis was unknown.

The reporter assessed the seriousness of cardiac failure as serious (disability and life-threatening).

The reporter assessed the seriousness of oedema peripheral as serious (disability) while did not assess the seriousness of arteriosclerosis.

The reporter did not assess the causality of arteriosclerosis while assessed the causality of cardiac failure and oedema peripheral in relationship to Eligard and Eligard unspecified device as not related.

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

Listedness:

Cardiac failure >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
Cardiac failure> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
Cardiac failure> Eligard®>unlisted as per USPI Eligard®>Feb-2025
Cardiac failure> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

oedema peripheral>Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
oedema peripheral> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
oedema peripheral> Eligard®>unlisted as per USPI Eligard®>Feb-2025
oedema peripheral> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

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

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding an elderly 78-year-old male patient who experienced serious events of 'heart failure' (cardiac failure) (life threatening) (medically significant) (permanent disability) and 'Lower Extremity Edema' (Oedema peripheral) (permanent disability) and a non-serious event of 'obstruction of the veins by fat' (Arteriosclerosis) during Eligard (leuprolide acetate) 45 mg therapy for prostate cancer. Tolmar assessed cardiac failure (life threatening) (medically significant) and Oedema peripheral (permanent disability) as serious and arteriosclerosis as non-serious since they did not meet the ICH seriousness criteria and are not IME events and Although Eligard is known to increase the risk of cardiovascular events like myocardial infarction and stroke, in this case, elderly age of the patient, co suspect drug Xtandi are strong confounders and hence reported events of cardiac failure, Oedema peripheral and arteriosclerosis are assessed as not related to Eligard (both drug and device).

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 of Admin : 1) Injection
Lot Number : 1) Unknown
Daily Dose : (45 milligram(s), 1 in 6 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates : 1) From : 10/May/2022 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) heart failure (Heart failure - 10019279, Cardiac failure - 10007554)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Lower Extremity Edema (Lower leg edema - 10078347, Oedema peripheral - 10030124)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) obstruction of the veins by fat (Arteriosclerosis - 10003210, Arteriosclerosis - 10003210)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) heart failure
CORE UnLabeled
2) Lower Extremity Edema
CORE UnLabeled
3) obstruction of the veins by fat
CORE UnLabeled

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) heart failure (Heart failure - 10019279, Cardiac failure - 10007554)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Lower Extremity Edema (Lower leg edema - 10078347, Oedema peripheral - 10030124)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) obstruction of the veins by fat (Arteriosclerosis - 10003210, Arteriosclerosis - 10003210)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) heart failure

Continuation Sheet for CIOMS report

CORE
2) Lower Extremity Edema
CORE
3) obstruction of the veins by fat
CORE

3) Drug	:	XTANDI
Active Substance	:	1) ENZALUTAMIDE
Drug Characterization	:	Suspect
Form of Admin	:	1) Capsule
Lot Number	:	1) Unknown
Daily Dose	:	(160 milligram(s), in 1 Day)
Route of Admin	:	1) Oral
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	1) From : 10/May/2022 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) heart failure (Heart failure - 10019279, Cardiac failure - 10007554)

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

2) Lower Extremity Edema (Lower leg edema - 10078347, Oedema peripheral - 10030124)

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

3) obstruction of the veins by fat (Arteriosclerosis - 10003210, Arteriosclerosis - 10003210)

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