

SUSPECT ADVERSE REACTION REPORT	
SV-TOLMAR, INC.-24SV046875	

## I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE Years	3. SEX	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
BAST	EL	Day	Month	Year	71	Male	Day	Month	Year	
		16	Nov	1952					2023	
Cont..										
7+13 DESCRIBE REACTION(S) (including relevant tests/lab data)										
1) HIS HEAD IS GETTING WORSE EVERY DAY (Memory impairment (10027175), Memory impairment (10027175)) Unknown										
2) Hair loss in the armpit (Hypotrichosis (10021126), Hypotrichosis (10021126)) ((//2023 - ) - Not Recovered/Not Resolved/Ongoing										
3) Menopausal hot flashes (Hot flashes (10020407), Hot flush (10060800)) ((//2023 - ) - Not Recovered/Not Resolved/Ongoing										
4) No sexual desire/ Zero sexual desire due to lack of testosterone (Libido decreased (10024419), Libido decreased (10024419)) ((//2023 - ) - Not Recovered/Not Resolved/Ongoing										Cont..
										<input type="checkbox"/> PATIENT DIED <input type="checkbox"/> LIFE THREATENING <input type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION <input type="checkbox"/> RESULTS IN PERSISTENCE OR SIGNIFICANT DISABILITY/INCAPACITY <input type="checkbox"/> CONGENITAL ANOMALY <input type="checkbox"/> OTHER MEDICALLY IMPORTANT CONDITION

## II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S)(include generic name)		20. DID EVENT ABATE AFTER STOPPING DRUG? <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA
1) Eligard® (Leuprolide acetate, Leuprolide acetate) (Suspect) (Injection)(Unknown)(Unknown)(Unknown)(Unknown) Cont..		
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 <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA (NA : Not Applicable)
17. INDICATION(S) FOR USE		
1) Prostate cancer [10060862 - Prostate cancer]		
18. THERAPY DATE(S) (from/to)		19. THERAPY DURATION
(-Jan-2024 - Ongoing)		

## III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
1) Radiotherapy( - /Oct/2023) <div style="text-align: right;">Cont..</div>
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)
1) PROSTATIC OPERATION (10061917, Prostatic operation) ((//2022 - ) <div style="text-align: right;">Cont..</div>

## IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		Study Information Study Name: NA EudraCT Number: Protocol No.: NA Center No.: Subject Id :
Name : Tolmar, Inc 701 Centre Avenue Fort Collins, CO, 80526, UNITED STATES OF AMERICA debbie.maierhofer@tolmar.comand+1-4129158447		
24. REPORT NULLIFIED	24b. MFR CONTROL NO.	
<input type="checkbox"/> YES <input type="checkbox"/> NO	SV-TOLMAR, INC.-24SV046875	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE	
22/May/2025	<input checked="" type="checkbox"/> STUDY <input type="checkbox"/> LITERATURE <input type="checkbox"/> HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE	
02/Jun/2025	<input checked="" type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOWUP	

= Continuation attached sheet(s)..

## Continuation Sheet for CIOMS report

## 1a. COUNTRY

EL SALVADOR

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

5) Sweating/ Menopausal sweating (Sweating (10042661), Hyperhidrosis (10020642)/(//2023 - ) - Not Recovered/Not Resolved/Ongoing)

6) TESTOSTERONE SUPPRESSION (Blood testosterone decreased (10005814), Blood testosterone decreased (10005814)/(Jan/2024 - ) - Not Recovered/Not Resolved/Ongoing)

## Event Description :

This Study report from EL SALVADOR was received by Adium (reference number: SV-ADIUM-SV-0007-20240209) on 09-FEB-2024 from a Consumer/ Other Non-Health Prof regarding an Elderly 71 Years old Male patient who experienced his head was getting worse every day (Memory impairment), Menopausal hot flashes (Hot flashes), Testosterone suppression (Blood testosterone decreased), No sexual desire (Libido decreased), Sweating (Sweating/Menopausal sweating) 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 12-FEB-2024.

The patient's medical history and current conditions included Prostate cancer, Blood pressure increased.

Concomitant medications included RADIOTHERAPY.

In JUL-2023, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration date: not reported). In JAN-2024, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration date: not reported). The patient had been experiencing side effects since receiving the second dose of Eligard in JAN-2024, including testosterone suppression, zero sexual desire, and menopausal hot flashes (feeling of intense heat) that cause sweating when seated (sweating). The doctor informed him that these symptoms were normal side effects of the Eligard medication, as it suppresses testosterone. The patient attributed some of the symptoms to his age, stating that he was already old. Aside from the mentioned symptoms, he did not have any additional symptoms and had not fully recovered from the aforementioned symptoms, which were still very frequent. The effects of the Eligard medication decreased over time, with the first application lasting about 4 to 5 months, becoming less frequent, occurring 1 or 2 times a day and eventually 1 or 2 times a week. On unknown date, he had received 20 radiation treatments for prostate cancer, with the last radiation in October 2023. He was still under cancer observation to check for possible metastasis in other parts of his body. On 15-FEB-2024, he was scheduled to undergo bone scans, CT scans, and regular monitoring. He recalled undergoing an examination involving a large machine but could not remember the name, attributing memory issues to age rather than the Eligard 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 Memory impairment was Unknown. The outcome of Hot flashes was Not Recovered/Not Resolved. The outcome of Blood testosterone decreased was Not Recovered/Not Resolved. The outcome of Libido decreased was Not Recovered/Not Resolved. The outcome of Sweating was Not Recovered/Not Resolved.

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

On 12-DEC-2024, follow up information was received by Adium (reference number: SV-ADIUM-SV-0007-20240209) from a consumer/Other Non-Health Prof and sent to Tolmar on 13-DEC-2024. New information included: Medical history: Prostatic operation, most recent dose of Eligard, and lab data were added, outcome of the event hot flashes updated to Recovering/Resolving (previously Not Recovered/Not Resolved).

On 12-DEC-2024, upon internal review added concomitant medication: OTHER THERAPEUTIC PRODUCTS (blood pressure medication) was added, medical history updated to Blood pressure high (from Blood pressure increased).

The patient's medical history and current conditions included Blood pressure high

Concomitant medications included OTHER THERAPEUTIC PRODUCTS (blood pressure medication).

On an unknown date, patient went to urinate 3 or 4 times at night and it was annoying, for that reason the urologist performed an ultrasound and indicated that he had a prostate between 4\*5 by 1 centimeter (huge), therefore, the doctor indicated to the patient that it would be good to reduce his prostate, he referred that in MAR or APR-2022 the operation for the reduction of the prostate was performed, then between 15 or 20 days later he received the results here he was diagnosed with cancer (which was inside the prostate). Patient did not present any symptoms. On an unknown date, 1 year ago (did not specify the date) the test was performed twice, which consists of putting the patient in a machine and verifying the bones, in both cases the results were negative. In JUL-2023, the first dose of Eligard was applied (the start date of therapy reported in the initial version (JUL- 2023) did not coincide with the date of the follow-up (OCT-2022), it was not modified), approximately the last dose was applied in JUL-2024, total patient received 3 doses of Eligard. In JUL-2024, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration date: not reported) (These dates do not coincide with the previous report and were not corrected according to previous notification). On an unknown date, since patient started treatment with Eligard patient had hot flashes, because patient assumed that the product suppresses testosterone and did not know if it was a female hormone or if it is the suppression of testosterone, for this reason patient had hot flashes as if she were in menopause, currently the hot flashes were gone down and that had a month to go before the third dose of Eligard runs out, therefore, patient thought that the hot flashes gone down and they had been going away because in the first dose the hot flashes were tremendous (sweating). Patient did not take any medication for the hot flashes, only used a fan to generate air and according to the doctor's recommendation and consumes a lot of water. On an unknown date, this week patient had to undergo a prostate antigen lab test and next week (date not specified) he had an appointment with his doctor. Previously, on an unknown date the result had been normal to this patient referred that it was relatively low. Corrective treatment was not taken for hot flashes. Action

## Continuation Sheet for CIOMS report

taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were not applicable. The outcome of Hot flashes was Recovering/Resolving.

## Relevant lab data included:

Unknown date: Prostatic specific antigen: low (values and ref range not provided).

Unknown date: Prostatic specific antigen: normal (values and ref range not provided).

Unknown date: Testosterone: suppressed (values and ref range not provided).

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

On 22-May-2025, follow up information was received by Adium. New information included: Added a new dose of Eligard. Added a new non-serious event of 'Loss of hair in armpit' (hypotrichosis). Updated Verbatim of event (hyperhidrosis) from 'sweating' to sweating/ menopausal sweating' and of (libido decreased) from 'no sexual desire' to 'no sexual desire/ zero sexual desire due to lack of testosterone. The outcome of event (hot flashes) was updated from 'recovering' to 'not resolved'. Event onset date of previously reported events was also updated.

On an unknown date, the patient received Eligard 45 mg, every 6 months via subcutaneous use for prostate cancer (Lot numbers and Expiration date: not reported)

On an unknown date and month in year 2023, the patient was continuing with symptoms of lot of sweats and menopausal hot flashes but later she had not experienced the sweat for a while, but on unknown date she had it again and she mentions that while watching TV without doing anything suddenly she had hot flashes like menopause and starts sweating. Additionally, the patient refers that the hairs in his armpits began to fall out, and according to the patient's words he only had 5 hairs, he does not know the cause, but he assumed that it was due to his age, as he gets older every year, he also mentioned that he had 4 applications of Eligard and he was expecting them to be last ones, his first injection was applied 2 years ago. The patient also referred that the lack of testosterone had caused him other problems including no sexual relations for 2 years and he assumed that it was due to suppression of testosterone that caused zero sexual desire. The patient clarified that the symptoms had begun to present since the first application of Eligard after 15 days of having it placed, he also mentioned that the only good thing was that now he shaves every 5 days and before he shaved every 2 days.

On an unknown date, in Jun-2025, the patient was expecting that the effect of Eligard will end, and he was expecting that at the appointment he will be able to take his last dose of Eligard. No further information was available.

On 25-Jun-2025, the patient was expecting an appointment in that he will be advised that he no longer needs any more injections and that he was no longer suffering from cancer, because he assumed that at that appointment they will only perform a prostate antigen test to validate the possibility of cancer, because he indicates that the Eligard injections were horrible as they cause him a very ugly sweatshirt, but he also assumes that it is also due to his age. No further details were provided.

Corrective treatment was unknown.

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

The outcome of hypotrichosis, hot flush, hyperhidrosis and libido decreased was not resolved.

The reporter did not assess the seriousness of hypotrichosis, hot flush, hyperhidrosis and libido decreased.

The reporter did not provide the causality of hypotrichosis, hot flush, hyperhidrosis and libido decreased in relationship to Eligard and Eligard Unspecified Device.

No follow up queries were raised.

Memory impairment>Eligard>Unlisted as per CCDS>07-Nov-2024

Memory impairment>Eligard>Unlisted as per USPI>Feb-2025

Memory impairment>Eligard unspecified device>Unlisted as per USPI>Feb-2025

Memory impairment>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Hypotrichosis>Eligard>Unlisted as per CCDS>07-Nov-2024

Hypotrichosis>Eligard>Unlisted as per USPI>Feb-2025

Hypotrichosis>Eligard unspecified device>Unlisted as per USPI>Feb-2025

Hypotrichosis>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Hot flush>Eligard>Listed as per CCDS>07-Nov-2024

Hot flush>Eligard>Listed as per USPI>Feb-2025

Hot flush>Eligard unspecified device>Listed as per USPI>Feb-2025

Hot flush>Eligard>Listed as per Canadian monograph>02-Apr-2025

Hyperhidrosis>Eligard>Listed as per CCDS>07-Nov-2024

Hyperhidrosis>Eligard>Listed as per USPI>Feb-2025

Hyperhidrosis>Eligard unspecified device>Listed as per USPI>Feb-2025

## Continuation Sheet for CIOMS report

Hyperhidrosis&gt;Eligard&gt;Listed as per Canadian monograph&gt;02-Apr-2025

Libido decreased&gt;Eligard&gt;Listed as per CCDS&gt;07-Nov-2024

Libido decreased&gt;Eligard&gt;Listed as per USPI&gt;Feb-2025

Libido decreased&gt;Eligard unspecified device&gt;Listed as per USPI&gt;Feb-2025

Libido decreased&gt;Eligard&gt;Listed as per Canadian monograph&gt;02-Apr-2025

Blood testosterone decreased&gt;Eligard&gt;Listed as per CCDS&gt;07-Nov-2024

Blood testosterone decreased&gt;Eligard&gt;Listed as per USPI&gt;Feb-2025

Blood testosterone decreased&gt;Eligard unspecified device&gt;Listed as per USPI&gt;Feb-2025

Blood testosterone decreased&gt;Eligard&gt;Listed as per Canadian monograph&gt;02-Apr-2025

## Company Remarks (Sender's Comments) :

This case is regarding an elderly 71 Years old Male patient who experienced Memory impairment ( his head was getting worse every day), Hot flashes ( Menopausal hot flashes), Blood testosterone decreased ( Testosterone suppression), Libido decreased ( No sexual desire), Sweating (Sweating/ Menopausal sweating), hypotrichosis (Loss of hair in armpit) during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. Tolmar assessed the reported events as non-serious since they did not meet the ICH seriousness criteria and are not IME events. Memory impairment event could be attributed to patient's elderly age and multiple radiotherapies which patient underwent. The causality for the events testosterone suppression, hot flushes, sweating, decreased libido and hypotrichosis can be attributed to Eligard use and assessed as related based on plausible temporality and known safety profile of the drug to cause testosterone suppression and eventual events. The reported events were assessed as not related to device component of Eligard.

## Additional Information (Continuation...)

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

1) Test Name: PSA

Result Unstructured Data (free text) : normal

Test Date:

2) Test Name: PSA

Result Unstructured Data (free text) : low

Test Date:

3) Test Name: TESTOSTERONE

Result Unstructured Data (free text) : suppressed

Test Date:

## Lab Comments :

1) Test Name : PSA

Lab Comments : normal

2) Test Name : PSA

Lab Comments : low

3) Test Name : TESTOSTERONE

Lab Comments : suppressed

## 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
	4) Injection
Lot Number	: 1) Unknown
	2) Unknown
	3) Unknown
	4) Unknown
Daily Dose	: (45 milligram(s), 1 in 6 Month)
	(45 milligram(s), 1 in 6 Month)
	(45 milligram(s), 1 in 6 Month)

## Continuation Sheet for CIOMS report

Route of Admin : (45 milligram(s), 1 in 6 Month)  
 : 1) Subcutaneous  
 : 2) Subcutaneous  
 : 3) Subcutaneous  
 : 4) Subcutaneous  
 Indications : 1) Prostate cancer [10060862 - Prostate cancer]  
 Action(s) Taken With Drug : Dose not changed

## Causality

- 1) HIS HEAD IS GETTING WORSE EVERY DAY (Memory impairment - 10027175, Memory impairment - 10027175 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 2) Hair loss in the armpit (Hypotrichosis - 10021126, Hypotrichosis - 10021126 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 3) Menopausal hot flashes (Hot flashes - 10020407, Hot flush - 10060800 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 4) No sexual desire/ Zero sexual desire due to lack of testosterone (Libido decreased - 10024419, Libido decreased - 10024419 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 5) Sweating/ Menopausal sweating (Sweating - 10042661, Hyperhidrosis - 10020642 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 6) TESTOSTERONE SUPPRESSION (Blood testosterone decreased - 10005814, Blood testosterone decreased - 10005814 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable

## Labeling :

- 1) HIS HEAD IS GETTING WORSE EVERY DAY  
 CORE UnLabeled
- 2) Hair loss in the armpit  
 CORE UnLabeled
- 3) Menopausal hot flashes  
 CORE Labeled
- 4) No sexual desire/ Zero sexual desire due to lack of testosterone  
 CORE Labeled
- 5) Sweating/ Menopausal sweating  
 CORE Labeled
- 6) TESTOSTERONE SUPPRESSION  
 CORE Labeled
- 2) Drug : Eligard® Unspecified Device (Leuprolide acetate)  
 Active Substance : 1) Leuprolide acetate  
 Drug Characterization : Suspect  
 Lot Number : 1) Unknown  
 Indications : 1) Prostate cancer [10060862 - Prostate cancer]  
 Action(s) Taken With Drug : Not applicable

## Causality

- 1) HIS HEAD IS GETTING WORSE EVERY DAY (Memory impairment - 10027175, Memory impairment - 10027175 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable

## Continuation Sheet for CIOMS report

- 2) Hair loss in the armpit (Hypotrichosis - 10021126, Hypotrichosis - 10021126 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 3) Menopausal hot flashes (Hot flashes - 10020407, Hot flush - 10060800 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 4) No sexual desire/ Zero sexual desire due to lack of testosterone (Libido decreased - 10024419, Libido decreased - 10024419 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 5) Sweating/ Menopausal sweating (Sweating - 10042661, Hyperhidrosis - 10020642 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable
- 6) TESTOSTERONE SUPPRESSION (Blood testosterone decreased - 10005814, Blood testosterone decreased - 10005814 )  
 Causality as per reporter : Not Reported  
 Causality as per Mfr : Not Related  
 DeChallenge : Not applicable  
 ReChallenge : Not Applicable

## Labeling :

- 1) HIS HEAD IS GETTING WORSE EVERY DAY  
CORE
- 2) Hair loss in the armpit  
CORE
- 3) Menopausal hot flashes  
CORE
- 4) No sexual desire/ Zero sexual desire due to lack of testosterone  
CORE
- 5) Sweating/ Menopausal sweating  
CORE
- 6) TESTOSTERONE SUPPRESSION  
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
- 4) 45 milligram, q 6 month

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

- 1). Drug : Radiotherapy  
 Form Strength :  
 Indications : 1) Prostate cancer [10060862 - Prostate cancer]  
 Therapy Dates : 1) From : To : /Oct/2023

- 2). Drug : OTHER THERAPEUTIC PRODUCTS  
 Active Substance : 1) blood pressure medication/Hypertension medication  
 Form Strength :  
 Daily Dose : 1) (1 dosage form, in 1 Day)  
 Indications : 1) high blood pressure [10020772 - Hypertension]

## 23. OTHER RELEVANT HISTORY (Continuation...)

- 2) PROSTATE CANCER (10060862 , Prostate cancer) (/2023 - ) (Continuing : YES )

Continuation Sheet for CIOMS report

3) BLOOD PRESSURE HIGH (10005747 , Blood pressure high) (Continuing : YES )