SUSPECT ADVERSE REACTION REPORT

DO-TOLMAR, INC.-24DO052159

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
L-R	DOMINICAN Cont..	02	Feb	1946	78	Male	28	Aug	2024

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

1) ISCHEMIC STROKE (Ischemic stroke (10055221), Ischaemic stroke (10061256))
(28/Aug/2024 -) - Not Recovered/Not Resolved/Ongoing
2) HEARING LOSS/ HE HEARS VERY LITTLE IN BOTH EARS (Hearing loss (10019246), Deafness (10011878))
(28/Aug/2024 -) - Not Recovered/Not Resolved/Ongoing
3) Memory loss (Memory loss (10027176), Amnesia (10001949))
(//2025 -) - Unknown
4) Right-sided hemiparesis (Hemiparesis (10019465), Hemiparesis (10019465))
(//2025 -) - 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) (24/Jan/2024 - Ongoing)	

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)

1)ENALAPRIL(ENALAPRIL)(20 Milligram)

Cont..

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

1) PROSTATE CANCER (10060862, Prostate cancer) (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	DO-TOLMAR, INC.-24DO052159
24c. DATE RECEIVED BY MANUFACTURER: 20/May/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 29/May/2025	25a. REPORT TYPE: ☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

1a. COUNTRY

DOMINICAN REPUBLIC

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

5) FLU (Flu (10016790), Influenza (10022000) - Not Recovered/Not Resolved/Ongoing)

6) SOMETIMES HE FORGETS THINGS/ Forgetfulness (Forgetfulness (10017060), Memory impairment (10027175) - Not Recovered/Not Resolved/ Ongoing)

7) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH (Sleep unwell (10041011), Poor quality sleep (10062519) - Not Recovered/Not Resolved/Ongoing)

8) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH/ cough (Cough (10011224), Cough (10011224) - Not Recovered/Not Resolved/Ongoing)

9) HE WAS VERY ILL (Illness (10080284), Illness (10080284) - Unknown)

Event Description :

This Study report from DOMINICAN REPUBLIC was received by Adium (reference number: DO-ADIUM-DO-0067-20240823) on 23-AUG-2024 from a Consumer regarding an Elderly 78-Year-old Male patient who experienced the events of Flu (Flu), Sometimes he forgets things (Forgetfulness), He could not sleep because he had a very strong cough (Sleep unwell), He could not sleep because he had a very strong cough (Cough), He was very ill (Illness), 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 23-AUG-2024.

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

Concomitant medications included Enalapril.

On 24-JAN-2024, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration dates were not reported). On an unknown date, unknown days after the most recent dose of Eligard, reported as 3 days ago, the patient had a flu and was very bad. The night before and last night, the patient could not sleep because he had a very strong cough, so he took only once a home remedy of aloe with bitter coffee which was strong and he was good and felt that it had done him good so far, because it took away the cough at once which was what bothered him the most. The patient was very ill when he arrived and took remedies and did not indicate which ones but noted that he was checked by a doctor from a clinic. The patient did not hear very well on one side (ear), from which the patient suffered before using the Eligard, but was listening well with his circumstances. The patient was going through a flu process, coughing, clawing and was making an effort to spit because of the flu secretion, a little severe, but nothing more. Corrective treatment included aloe with bitter coffee. Action taken with Eligard in response to the events was Unknown. De-challenge and re-challenge were not applicable. The outcome of Flu was Not Recovered/Not Resolved. The outcome of Forgetfulness was Not Recovered/Not Resolved. The outcome of Sleep unwell was Not Recovered/Not Resolved. The outcome of Cough was Not Recovered/Not Resolved. The outcome of Illness was Unknown.

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

On 03-SEP-2024, upon internal review, the event of respiratory tract congestion was removed. No further changes were performed.

On 18-FEB-2025, follow-up information was received by Adium via patient support program (reference number: DO-ADIUM-DO-0067-20240823) from a Consumer/Other Non-Health Prof Consumer and sent to Tolmar on 19-FEB-2025. New information included: Case upgraded to serious, serious (medically significant) event Ischemic stroke (Ischemic stroke) added, serious (medically significant) event of hearing loss/ he hears very little in both ears (Hearing loss) added, concomitant medications, medical history, most recent dose of Eligard, action taken, laboratory details and clinical course.

The patient's medical history and current conditions included Malaise and Myalgia.

Concomitant medications included enalapril, Cardio-Kd (hydrochlorothiazide, valsartan) and Citopril.

On 28-AUG-2024, after an unspecified amount of time from the most recent dose of Eligard, the patient experienced Ischemic stroke which resulted in hearing loss, he was able to hear very little in both ears. The patient was being treated for hearing loss but at the reporting time in his own country he had not yet been treated. He would have to have an appointment with neurologist before being scheduled with the otorhinolaryngologist. In SEP-2024, the patient had CT scan through which the neurologist indicated that it was unnecessary to repeat it because the patient was progressing satisfactorily. On unspecified date in SEP-2024 or OCT-2024, the patient received Eligard 22.5 milligram, q 3 month via Subcutaneous use (Lot numbers: unknown; Expiration date: unknown). Further corrective treatment was not reported. The patient's next Eligard injection was scheduled for 10-MAY-2025. Action taken with Eligard in response to the events was Dose not changed. De-challenge and re-challenge were not applicable. The outcome of Ischemic stroke was Not recovered/ Not resolved. The outcome of Hearing loss was Not recovered/ Not resolved.

Relevant test results included:
SEP-2024: Computerized tomogram: results not reported.

Continuation Sheet for CIOMS report

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

On 20-May-2025, follow-up information was received by Adium via patient support program (reference number: DO-ADIUM-DO-0067-20240823) from a Consumer/Other Non-Health Professional (patient's family member). This report was sent to Tolmar on 21-May-2025. New information included: added serious events (medically significant) (hospitalization) (disability) ‘memory loss' (Amnesia) and ‘right-side hemiparesis' (Hemiparesis), seriousness of ischemic stroke was upgraded to disability/incapacity and hospitalisation. Verbatim of event ‘cough' was updated from ‘he could not sleep because of strong cough' to ‘he could not sleep because of strong cough/ cough' and Verbatim of event ‘forgetfulness' was updated from ‘sometimes he forgets things' updated to ‘sometimes he forgets things/ forgetfulness'. Narratives was updated.

On an unknown date and month in 2025, patient's family member reported that patient was hospitalized due to memory loss (Amnesia) and right-side hemiparesis (Hemiparesis) as a result of ischemic stroke. The intensity of these events was reported as severe. It was reported that the sign or symptom experienced to be not related to the product administered.

On an unknown date, the patient was discharged from the hospital.

Corrective treatment include hospitalization.

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

The outcome of amnesia was unknown and hemiparesis was not recovered.

The reporter assesses the seriousness of amnesia and hemiparesis as serious (medically significant) (hospitalization) (disability).

The reporter assessed the causality of amnesia and hemiparesis in relationship to Eligard and Eligard unspecified device as not related.

No further information is expected as the reporter did not consent to be contacted for follow-up.

Listedness of previously reported events cerebrovascular accident, cough, flu, sleep unwell, forgetfulness, illness and hearing loss.
Amnesia >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
Amnesia > Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
Amnesia > Eligard®>unlisted as per USPI Eligard®>Feb-2025
Amnesia > Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Hemiparesis >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
Hemiparesis > Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
Hemiparesis > Eligard®>unlisted as per USPI Eligard®>Feb-2025
Hemiparesis > 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 influenza (Flu), memory impairment (Sometimes he forgets things), poor quality sleep (He could not sleep because he had a very strong cough), cough (He could not sleep because he had a very strong cough), illness (He was very ill), ischemic stroke (ischemic stroke) and deafness (hearing loss/he hears very little in both ears) during Eligard (Leuprolide acetate) 22.5 mg therapy for prostate cancer. Tolmar assessed the event ischemic stroke as serious (MS) as it is an IME event, it resulted in hospitalisation and also caused disability and requires significant medical intervention to prevent a serious outcome, deafness is a serious event (MS) as it is an IME event, while all other events are considered as non-serious as they did not meet ICH seriousness criteria. Ischemic stroke is considered as related to Eligard (drug) based on the inferred temporal relationship and consistency of the event with product safety profile, while all other events are considered as not related to Eligard (drug). Cough, poor quality sleep, illness are due to flu. Elderly age and underlying malignancy are considered as confounders for flu, ischemic stroke and memory impairment. All the events are not related to device component.

FU added event of hemiparesis (right sided hemiparesis) and amnesia (memory loss). Tolmar assessed the reported events as serious as they resulted in hospitalisation
and caused disability. The causality of the events hemiparesis and amnesia was assessed as not related to suspect Eligard(drug and device) considering the nature of event, aetiopathogenesis, inconsistency with the safety profile of the drug and these events could be secondary to cerebrovascular accident, history of hypertension and elderly could be a risk factors for the events.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
CT SCAN	/Sep/2024		

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

Continuation Sheet for CIOMS report

1) Test Name: CT SCAN

Result Unstructured Data (free text) : Results not reported

Test Date: /Sep/2024

Lab Comments :

1) Test Name : CT SCAN

Lab Comments : Results not reported

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 : 24/Jan/2024 To :Continuing
		2) From : //2024 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) ISCHEMIC STROKE (Ischemic stroke - 10055221, Ischaemic stroke - 10061256)

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

2) HEARING LOSS/ HE HEARS VERY LITTLE IN BOTH EARS (Hearing loss - 10019246, Deafness - 10011878)

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

3) Memory loss (Memory loss - 10027176, Amnesia - 10001949)

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

4) Right-sided hemiparesis (Hemiparesis - 10019465, Hemiparesis - 10019465)

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

5) FLU (Flu - 10016790, Influenza - 10022000)

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

6) SOMETIMES HE FORGETS THINGS/ Forgetfulness (Forgetfulness - 10017060, Memory impairment - 10027175)

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

7) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH (Sleep unwell - 10041011, Poor quality sleep - 10062519)

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

Continuation Sheet for CIOMS report

ReChallenge : Not Applicable

8) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH/ cough (Cough - 10011224, Cough - 10011224)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

9) HE WAS VERY ILL (Illness - 10080284, Illness - 10080284)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) ISCHEMIC STROKE
CORE Labeled
2) HEARING LOSS/ HE HEARS VERY LITTLE IN BOTH EARS
CORE UnLabeled
3) Memory loss
CORE UnLabeled
4) Right-sided hemiparesis
CORE UnLabeled
5) FLU
CORE UnLabeled
6) SOMETIMES HE FORGETS THINGS/ Forgetfulness
CORE UnLabeled
7) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH
CORE UnLabeled
8) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH/ cough
CORE UnLabeled
9) HE WAS VERY ILL
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) ISCHEMIC STROKE (Ischemic stroke - 10055221, Ischaemic stroke - 10061256)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) HEARING LOSS/ HE HEARS VERY LITTLE IN BOTH EARS (Hearing loss - 10019246, Deafness - 10011878)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Memory loss (Memory loss - 10027176, Amnesia - 10001949)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Right-sided hemiparesis (Hemiparesis - 10019465, Hemiparesis - 10019465)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) FLU (Flu - 10016790, Influenza - 10022000)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) SOMETIMES HE FORGETS THINGS/ Forgetfulness (Forgetfulness - 10017060, Memory impairment - 10027175)

Continuation Sheet for CIOMS report

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

7) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH (Sleep unwell - 10041011, Poor quality sleep - 10062519)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

8) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH/ cough (Cough - 10011224, Cough - 10011224)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

9) HE WAS VERY ILL (Illness - 10080284, Illness - 10080284)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) ISCHEMIC STROKE
CORE
2) HEARING LOSS/ HE HEARS VERY LITTLE IN BOTH EARS
CORE
3) Memory loss
CORE
4) Right-sided hemiparesis
CORE
5) FLU
CORE
6) SOMETIMES HE FORGETS THINGS/ Forgetfulness
CORE
7) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH
CORE
8) HE COULD NOT SLEEP BECAUSE HE HAD A VERY STRONG COUGH/ cough
CORE
9) HE WAS VERY ILL
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

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

1). Drug : ENALAPRIL
Active Substance : 1) ENALAPRIL
Form Strength : 1) 20 Milligram
Daily Dose : 1) (20 milligram(s), 1 in 1 Day)
Indications : 1) high blood pressure [10020772 - Hypertension]

2). Drug : CARDIO-KD
Active Substance : 1) HYDROCHLOROTHIAZIDE
2) VALSARTAN
Form Strength :
Daily Dose : 1) (1 in 1 Day)
Indications : 1) hypertension [10020772 - Hypertension]

3). Drug : ALOE VERA
Active Substance : 1) ALOE VERA

Continuation Sheet for CIOMS report

Form Strength :
Indications : 1) Strong cough [10011224 - Cough]

23. OTHER RELEVANT HISTORY (Continuation...)

2) HYPERTENSION (10020772 , Hypertension) (Continuing : YES)

3) HEARING IMPAIRED (10019245 , Hearing impaired) (Continuing : YES)

4) MUSCLE PAIN (10028322 , Muscle pain) (Continuing : YES)

5) DISCOMFORT (10013082 , Discomfort)