SUSPECT ADVERSE REACTION REPORT

DO-TOLMAR, INC.-22DO037090

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
RRPG	DOMINICAN Cont..	12	Nov	1951	70	Male			2022

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

1) cataract surgery in both eyes (Cataract (10007739), Cataract (10007739))
(//2022 -) - Not Recovered/Not Resolved/Ongoing
2) Infectious ulcer in the eye (Infective corneal ulcer (10075400), Infective corneal ulcer (10075400))
(19/Aug/2024 -) - Not Recovered/Not Resolved/Ongoing
3) problem in the cornea (Corneal disorder (10061453), Corneal disorder (10061453))
Not Recovered/Not Resolved/Ongoing
4) When he urinates he feels an odor like horse urine (Urine odor abnormal (10074143), Urine odour abnormal (10057135))
(/Aug/2022 -) - 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) (45 Milligram, Injection)(Unknown)(45 Milligram, Injection)(Unknown)(45 Milligram, Injection)(Unknown)(45 Milligram, Injection)(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

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
(29-Aug-2022 -)	

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)DOLO-NEUROBION N [CYANOCOBALAMIN;DICLOFENAC SODIUM;PYRIDOXINE HYDROCHLORIDE;THIAMINE](CYANOCOBALAMIN)

Cont..

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

1) PROSTATE SURGERY (10073343, Prostate surgery) (04/Nov/2021 -) (Continuing: No)

Cont..

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	24b. MFR CONTROL NO.
☐ YES ☐ NO	DO-TOLMAR, INC.-22DO037090
24c. DATE RECEIVED BY MANUFACTURER: 14/Jul/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 17/Jul/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) Change of medication (Therapy change (10074300), Therapy change (10074300)(//2024 -) - Unknown)

6) Patient indicates that his medication was changed to Triana (Therapy cessation (10065154), Therapy cessation (10065154)(//2024 -) - Unknown)

7) a problem in his left ear (Ear disorder (10014004), Ear disorder (10014004) - Recovering/Resolving)

Event Description :

This Study report from DOMINICAN REPUBLIC was received by Adium (reference number: DO-0128-20221014) via the Patient Support Program "ASOFARMA A TU LADO" on 13-OCT-2022 from a Consumer regarding an Elderly 70 Years old Male patient who experienced When he urinates, he feels an odor like horse urine (Urine odor abnormal) 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 14-OCT-2022.

The patient's medical history included: Back pain (for several years) and Hypertension for 20 years (exact date unknown). Procedure included Prostate surgery (Operated for prostate cancer on 4 November 2021).
Current conditions included: Prostate cancer.

Concomitant medications included: DOLO-NEUROBION for back pain (every 6 or 8 hours for 2 days), AMLODIPINE for High blood pressure (5 mg half a capsule a day) and CARVEDILOL for High blood pressure (12.5 mg half a capsule a day).

In AUG-2022, the patient began receiving Eligard 45 milligram, q 6 month, via Subcutaneous use, for Prostate cancer (Lot number(s) and Expiration date details not provided). In Aug 2022 after the most recent dose of Eligard, (reporter as after two or three days; exact date not provided), when the patient had urinated felt an odor like horse urine (urine odor abnormal) and that the patient does not know if it is due to the medication and if it is normal. Corrective treatment was not reported. Action taken with Eligard in response to the events was Dose Not Changed. De-challenge was Not Applicable, and Re-challenge was Not Applicable. The outcome of Urine odor abnormal was Not Recovered/Not Resolved.

The reporter did not assess the seriousness of the event and assessed the causality in relationship to Eligard as Not Reporter.

On 19-SEP-2024, follow up information was received by Adium (reference number: DO-0128-20221014) via the Patient Support Program from a consumer/Other Non-Health Prof. New information included new serious events of cataract surgery in both eyes (Cataract) (Medically significant, Disability), problem in the cornea (corneal disorder) (Medically significant), Infectious ulcer in the eye (Infective corneal ulcer) (Medically significant), new non-serious event of Left ear problem (Ear disorder), most recent dose of Eligard, Treatment information, lab data were added, Eligard therapy start date updated. Case was upgraded to serious.

On an unknown date in 2022 (reported as 2 years ago), time to unknown onset after the start of Eligard, patient had cataract surgery in both eyes, but he was still in the process of recovery because on an unknown date, he had a problem in the cornea that did not allow him to see completely well. As his vision was not very good, the ophthalmologist told him that he must continue applying the drops for 1 year, he did not indicate the names. For this reason, when he was walking down the street, he could not do it alone but must have been accompanied to run errands. On an unspecified dates, the patient received 3 subsequent doses of Eligard 45 milligram, q 6 month, via Subcutaneous use, for Prostate cancer (Lot numbers and Expiration dates not provided). The patient mentioned that the last Eligard application he had was 6 months ago. Since an unknown date in 2024, at an unknown amount of time after the most recent dose of Eligard, the patient had problems with vision because in the consultation with the eye doctor, they poked his eye because he had an infection that he said it was an infectious ulcer. He was prescribed with some drops (unspecified), he did not remember the names, only that he applied them every 20 minutes 1 drop in each eye, 1 to 4 times a day, and the other drops, he did not remember the name, he applied them 3 times a day, for this reason, he could not see the telephone. As he could not see telephone, for 1 month (did not refer date), he had medical leave and on unspecified date (reported as Saturday) it was lifted, because on 19-SEP-2024 he would be one month old. On an unknown date, he underwent vitamin D tests, because 1 week prior to reporting date, he had a problem in his left ear. On 16-SEP-2024 (reported as Monday), he had his left ear washed, and he was feeling better now. The next Eligard application would be on 19-SEP-2024 or 20-SEP-2024, depending on the insurance authorization, and that with the next application, he would have 5 because it is applied every 6 months. Corrective treatment for cataract, corneal disorder and Infective corneal ulcer was eye drops (unspecified). Correction treatment for Ear disorder was left ear wash. Action taken with Eligard in response to the events was Dose Not Changed. De-challenge was Not Applicable, and Re-challenge was Not Applicable. The outcome of Infective corneal ulcer was Not Recovered/Not Resolved. The outcome of Cataract was Not Recovered/Not Resolved. The outcome of Corneal disorder was Not Recovered/Not Resolved. The outcome of Ear disorder was Recovering/Resolving.

Relevant lab tests included:
Unknown date (2024), Vitamin D: Result and values not provided.

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

On 14-Jul-2025, the follow up information was received by Adium via "ASOFARMA A TU LADO" the Patient Support Program (reference number: DO-0128-20221014 (2)) from a consumer (non-healthcare professional) and sent to Tolmar on 15-Jul-2025. New information included: added patient demographics (height and weight) and onset date of prostate cancer. Added new non-serious events of "medication change" (therapy change) and

Continuation Sheet for CIOMS report

"Patient indicates that his medication was changed to Triana" (Therapy cessation). Updated action taken from "dose not changed" to "unknown". Narrative was updated.

On an unknown date in 2024, the patient indicates that his medication was changed to Triana. No further information was reported.

Corrective treatment was not reported.

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

The outcome of therapy change, and therapy cessation was unknown.

The reporter assessed the seriousness of therapy change as non-serious and did not assess the seriousness of therapy cessation.

The reporter assessed the causality of therapy change and therapy cessation in relationship to Eligard and Eligard unspecified device as not related.

No further queries were raised.

Listedness of previously reported events cataract, corneal disorder, Infective corneal ulcer, urine odour abnormal and ear disorder were retained as previously assessed.
therapy change >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
therapy change> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
therapy change> Eligard®>unlisted as per USPI Eligard®>Feb-2025
therapy change> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

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

Company Remarks (Sender's Comments) :

Evaluator Comment (Tolmar): This 70 years old male patient had Cataract (cataract surgery in both eyes), Corneal disorder (problem in the cornea), Infective corneal ulcer (Infectious ulcer in the eye), Ear disorder (a problem in his left ear) and Urine odour abnormal (When he urinates he feels an odor like horse urine) during Eligard (Leuprolide acetate) 45 milligram therapy for Prostate cancer. Tolmar assessed Cataract, corneal disorder and infective corneal ulcer as medically significant based on their nature and cataract was also serious due to disability (in line with the reporter's assessment); the remaining events as non-serious since there was no immediate jeopardy to patient and 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. Elderly age confounds Cataract. Assessment was done based on limited available information only and could be revised when follow-up becomes available.

FU added events therapy change (medication change) and Therapy cessation (Patient indicates that his medication was changed to Triana). Tolmar assessed the reported events as non-serious since they did not meet the ICH seriousness criteria. The causality of therapy change and therapy cessation was assessed as not related to suspect Eligard(drug and device) as the events occurred due to human action rather than due to drug.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
VITAMIN D	//2024		

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

1) Test Name: VITAMIN D

Result Unstructured Data (free text) : Notes: result not provided
Test Date: //2024
Lab Comments :

1) Test Name : VITAMIN D
Lab Comments : result not provided

14.SUSPECT DRUG(S) (Continuation...)

Product-Reaction Level

Continuation Sheet for CIOMS report

1) Drug	:	Eligard® (Leuprolide acetate)
Active Substance	:	1) Leuprolide acetate
Drug Characterization	:	Suspect
Form Strength	:	1) 45 Milligram
		2) 45 Milligram
		3) 45 Milligram
		4) 45 Milligram
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)
		(45 milligram(s), 1 in 6 Month)
Route of Admin	:	1) Subcutaneous
		2) Subcutaneous
		3) Subcutaneous
		4) Subcutaneous
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	4) From : To ://2024
Action(s) Taken With Drug	:	Unknown

Causality

1) cataract surgery in both eyes (Cataract - 10007739, Cataract - 10007739)

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

2) Infectious ulcer in the eye (Infective corneal ulcer - 10075400, Infective corneal ulcer - 10075400)

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

3) problem in the cornea (Corneal disorder - 10061453, Corneal disorder - 10061453)

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

4) When he urinates he feels an odor like horse urine (Urine odor abnormal - 10074143, Urine odour abnormal - 10057135)

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

5) Change of medication (Therapy change - 10074300, Therapy change - 10074300)

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

6) Patient indicates that his medication was changed to Triana (Therapy cessation - 10065154, Therapy cessation - 10065154)

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

7) a problem in his left ear (Ear disorder - 10014004, Ear disorder - 10014004)

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

Continuation Sheet for CIOMS report

Labeling :

1) cataract surgery in both eyes
CORE UnLabeled
2) Infectious ulcer in the eye
CORE UnLabeled
3) problem in the cornea
CORE UnLabeled
4) When he urinates he feels an odor like horse urine
CORE UnLabeled
5) Change of medication
CORE UnLabeled
6) Patient indicates that his medication was changed to Triana
CORE UnLabeled
7) a problem in his left ear
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
Route of Admin : 1) Unknown
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

1) cataract surgery in both eyes (Cataract - 10007739, Cataract - 10007739)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Infectious ulcer in the eye (Infective corneal ulcer - 10075400, Infective corneal ulcer - 10075400)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) problem in the cornea (Corneal disorder - 10061453, Corneal disorder - 10061453)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) When he urinates he feels an odor like horse urine (Urine odor abnormal - 10074143, Urine odour abnormal - 10057135)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
5) Change of medication (Therapy change - 10074300, Therapy change - 10074300)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
6) Patient indicates that his medication was changed to Triana (Therapy cessation - 10065154, Therapy cessation - 10065154)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
7) a problem in his left ear (Ear disorder - 10014004, Ear disorder - 10014004)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) cataract surgery in both eyes
CORE
2) Infectious ulcer in the eye

Continuation Sheet for CIOMS report

CORE
3) problem in the cornea
CORE
4) When he urinates he feels an odor like horse urine
CORE
5) Change of medication
CORE
6) Patient indicates that his medication was changed to Triana
CORE
7) a problem in his left ear
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

Drug 2 :Eligard® Unspecified Device

1) UNK

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

1). Drug	:	DOLO-NEUROBION N [CYANOCOBALAMIN;DICLOFENAC SODIUM;PYRIDOXINE HYDROCHLORIDE;THIAMINE]
Active Substance	:	1) CYANOCOBALAMIN 2) DICLOFENAC SODIUM 3) PYRIDOXINE HYDROCHLORIDE 4) THIAMINE
Form Strength	:	
Route of Admin	:	1) Oral
Indications	:	1) Back pain [10003988 - Back pain]
Dosage Text	:	1) every 6 or 8 hours for 2 days

2). Drug	:	AMLODIPINE
Active Substance	:	1) AMLODIPINE
Form Strength	:	
Daily Dose	:	1) 5 milligram(s) (5 milligram(s), 1 in 1 Day)
Route of Admin	:	1) Unknown
Indications	:	1) High blood pressure [10005747 - Blood pressure high]
Dosage Text	:	1) half a capsule a day

3). Drug	:	CARVEDILOL
Active Substance	:	1) CARVEDILOL
Form Strength	:	
Daily Dose	:	1) 12.5 milligram(s) (12.5 milligram(s), 1 in 1 Day)
Route of Admin	:	1) Unknown
Indications	:	1) High blood pressure [10005747 - Blood pressure high]
Dosage Text	:	1) half a capsule a day

23. OTHER RELEVANT HISTORY (Continuation...)

2) PROSTATE CANCER (10060862 , Prostate cancer) (//2022 -) (Continuing : YES)

3) BACK PAIN (10003988 , Back pain) (Continuing : Unknown)

4) HIGH BLOOD PRESSURE (10005747 , Blood pressure high)