CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

DO-TOLMAR, INC.-24DO049361

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
		Day	Month	Year			Day	Month	Year	
BUM	DOMINICAN Cont..	14	Jun	1934	89	Male				

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

1) PATIENT WAS WALKING AND THEN SAT DOWN AND DIED THERE (Death (10011906), Death (10011906))
(- 09/Jan/2025) - Fatal
2) heart attack (Heart attack (10019250), Myocardial infarction (10028596))
Unknown
3) THE PATIENT IS GIVEN THE ELIGARD MEDICATION ANNUALLY (Off label dosing frequency (10076395), Off label use (10053762))
Unknown

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

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

Cont..

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] NA

15. DAILY DOSE(S)

(45 milligram(s))

(45 milligram(s))

16. ROUTE(S) OF ADMINISTRATION

21. DID EVENT REAPPEAR AFTER REINTRODUCTION [ ] YES [ ] NO [x] NA

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Prostate Cancer [10060862 - Prostate cancer]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (11/Feb/2024 -)	

III. CONCOMITANT DRUG(S) AND HISTORY

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

1)RADIOTHERAPY(RADIOTHERAPY)

Cont..

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

1) PROSTATE CANCER (10060862, Prostate cancer) (Asked but Unknown -) (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.-24DO049361
24c. DATE RECEIVED BY MANUFACTURER: 09/Apr/2025	24d. REPORT SOURCE: [x] STUDY [ ] LITERATURE [ ] HEALTH PROFESSIONAL
DATE OF THIS REPORT: 19/Apr/2025	25a. REPORT TYPE: [x] 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...)

Event Description :

This Study report from DOMINICAN REPUBLIC was received by Adium via Patient Support Program "ASOFARMA A TU LADO" (reference number: DO-ADIUM-DO-0033-20240513) on 13-MAY-2024 from a Consumer/Other Non-Health Prof regarding an Elderly 89- year-old Male patient who was given the Eligard medication annually (Off label dosing frequency), 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-MAY-2024.

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

Concomitant medications included: RADIOTHERAPY. OTHER THERAPEUTIC PRODUCTS (Datafludo medication 500mg)

On 05-MAR-2024, the patient began receiving Eligard 45 milligram via Subcutaneous use for Prostate cancer (Lot details and Expiration date: were not reported). the patient was given the Eligard medication annually, it was the first dose given to the patient for one year, as indicated by the Doctor, that before the patient was given Eligard every 3 months, then every 6 months, but in this last application it was for one year because the Doctor told the patient that the reason was because the free PSA was fine (at the levels it should be), after the radiotherapies had been performed. They did not know if the patient would continue to take the Eligard medication every year or if he would take it again every 6 months. The next dose of Eligard would be in February or March 2025. Datafludo medication 500mg (unknown medication) tablets: patient used it permanently so he can urinate well. Patient was using this medication before starting the Eligard medication.
Action taken with Eligard in response to the event was Unknown. De-challenge was Unknown, and re-challenge was Unknown.
The outcome of Off label dosing frequency was Unknown.

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

On 22-JAN-2025, follow-up information was received by ADIUM (reference number: DO-ADIUM-DO-0033-20240513) from a Consumer/Other Non-Health Prof and sent to Tolmar on 23-JAN-2025. New information included New Serious (Fatal) event of Death, Eligard therapy details, Historical drug details were added.

The patient's medical history and current conditions included ELIGARD 22.5 mg.

On an unknown date, the patient received first dose of Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration dates were Not provided).

On an unknown date, the patient received second dose of Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration dates were Not provided).

On 05-MAR-2024 (also reported as 19-FEB-2024), the patient began receiving Eligard 45 milligram annually via Subcutaneous use for Prostate cancer (Lot details and Expiration date: were not reported). The next Eligard 45 mg dose would be administered in FEB-2025.

Reportedly, on 09-JAN-2025, the patient was walking and then sat down and died. Cause of death was unknown. It was unknown whether autopsy was performed. The patient was 90-Year-old at time of death. Corrective treatment was not reported. Action taken with Eligard in response to the events was Not Applicable. De-challenge and re-challenge were Not applicable. The outcome of Death was Fatal.

The reporter assessed the seriousness of Death as serious (Fatal) and did not asses the causality of the event in relationship to Eligard.

On 09-Apr-2025, the follow up information was received via Adium (reference number: DO-ADIUM-DO-0033-20240513) from a patient's daughter (consumer or non-healthcare professional) and sent to Tolmar on 10-Apr-2025. New information included: New current conditions- 'urinary retention' and blockade (Urinary tract obstruction) were added. A new serious (medically significant) event ‘heart attack' (myocardial infarction) was added. primary dose detail added and narrative updated.

The patient's medical history was unknown and current condition included urinary retention and urinary tract obstruction.

On 13-Feb-2023, the patient received his first dose of Eligard 45mg. The expiration date and lot number are missing because the location where the medication was administered does not provide this information (CRM start date maintained).

On 11-Feb-2024. the patient received his last dose of Eligard 45 mg.

On an unknown date, the patient experienced heart attack.

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

The outcome of myocardial infarction was unknown.

Continuation Sheet for CIOMS report

The reporter did not assess the seriousness of myocardial infarction.

The reporter did not provide the causality of myocardial infarction in relationship to Eligard and Eligard Unspecified Device.

It was reported that the patient's daughter agrees to be contacted and to contact the treating physician for future follow-up.

Listedness
Labeling of previously assessed events is retained as reported in the as determined listedness section of Product event assessment.

Myocardial infarction>Eligard® >listed as per CCDS Eligard®> 7-Nov-2024
Myocardial infarction> Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025
Myocardial infarction> Eligard®>listed as per USPI Eligard®>Feb-2025
Myocardial infarction> Eligard® Unspecified Device> listed as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Evaluator Comment (Tolmar): This is regarding an elderly 89-year-old male patient who was given the Eligard medication annually (Off label dosing frequency) during Eligard (Leuprolide acetate) 45 mg therapy for prostate cancer. Patient passed away (patient was walking and then sat down and died there). Tolmar assessed death of the patient as serious due to fatal outcome. Off label use is non-serious as it did not meet ICH seriousness criteria. Causal association of death with Eligard (drug) is not assessable as the information provided is limited, cause of death, autopsy details is not reported and relevant medical history, concomitant medications and events or circumstances preceding patient's death is not reported. Elderly age and underlying malignancy are pre-existing risk factors for patient's death. Death is not related to device component. Off label use is due to human action, hence considered as not related to Eligard (drug and device). Fu added event of myocardial infarction (heart attack). Tolmar assessed the event myocardial infarction was assessed as serious as it is included in IME list. The causality of event myocardial infarction was assessed as not related to suspect Eligard(drug and device) as causal role of the drug could not be fully established with limited available information including lack of details on relevant medical history. Hypercoagulable state due to cancer and elderly age were the risk factors

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

Product-Reaction Level

1) Drug	:	Eligard® (Leuprolide acetate)
Active Substance	:	1) Leuprolide acetate
Drug Characterization	:	Suspect
Form of Admin	:	3) Injection 4) Injection
Lot Number	:	3) Unknown 4) Unknown
Daily Dose	:	(45 milligram(s)) (45 milligram(s)) (45 milligram(s), 1 in 6 Month) (45 milligram(s), 1 in 6 Month)
Route of Admin	:	3) Subcutaneous 4) Subcutaneous
Indications	:	1) Prostate Cancer [10060862 - Prostate cancer]
Therapy Dates	:	1) From : 11/Feb/2024 To :Not applicable 2) From : 13/Feb/2023 To :Not applicable
Action(s) Taken With Drug	:	Not applicable

Causality

1) PATIENT WAS WALKING AND THEN SAT DOWN AND DIED THERE (Death - 10011906, Death - 10011906)

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

2) heart attack (Heart attack - 10019250, Myocardial infarction - 10028596)

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

3) THE PATIENT IS GIVEN THE ELIGARD MEDICATION ANNUALLY (Off label dosing frequency - 10076395, Off label use - 10053762)

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

Continuation Sheet for CIOMS report

DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) PATIENT WAS WALKING AND THEN SAT DOWN AND DIED THERE
CORE UnLabeled
2) heart attack
CORE UnLabeled
3) THE PATIENT IS GIVEN THE ELIGARD MEDICATION ANNUALLY
CORE UnLabeled

2) Drug : Eligard® Unspecified Device (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form of Admin : 1) Injection
Indications : 1) Prostate Cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

1) PATIENT WAS WALKING AND THEN SAT DOWN AND DIED THERE (Death - 10011906, Death - 10011906)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) heart attack (Heart attack - 10019250, Myocardial infarction - 10028596)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) THE PATIENT IS GIVEN THE ELIGARD MEDICATION ANNUALLY (Off label dosing frequency - 10076395, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) PATIENT WAS WALKING AND THEN SAT DOWN AND DIED THERE
CORE
2) heart attack
CORE
3) THE PATIENT IS GIVEN THE ELIGARD MEDICATION ANNUALLY
CORE

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

Dosage Text :

Drug 1 :Eligard®

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 : RADIOTHERAPY
Active Substance : 1) RADIOTHERAPY
Form Strength :
Indications : 1) Drug use for unknown indication [10057097 - Drug use for unknown indication]
Dosage Text : 1) UNK

2). Drug : Datafludo
Form Strength :
Daily Dose : 1) 500.0 milligram(s) (500 milligram(s), 1 in 1 Day)
Indications : 1) urinary retention [10046555 - Urinary retention]

Continuation Sheet for CIOMS report

		2) blockage [10061574 - Urinary tract obstruction]
Dosage Text	:	1) UNK

23. OTHER RELEVANT HISTORY (Continuation...)

2) URINARY RETENTION (10046555 , Urinary retention) (Continuing : YES)

3) BLOCKAGE (10046548 , Urinary obstruction unspecified) (Continuing : YES)

Past Therapy (ies)

Product Name	:	ELIGARD
Indication	:	Prostate cancer (10060862)
Start Date	:	13/Jan/2023
Stop Date	:	