SUSPECT ADVERSE REACTION REPORT

DO-TOLMAR, INC.-22DO036196

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
LAH	DOMINICAN Cont..	13	Dec	1947	77	Male			

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

1) STAGE 5 DUE TO PROSTATE CANCER AND WITH METASTASIS (Prostate cancer metastatic (10036909), Prostate cancer metastatic (10036909))
Not Recovered/Not Resolved/Ongoing
2) ELEVATED PSA (Prostatic specific antigen increased (10036975), Prostatic specific antigen increased (10036975))
Unknown
3) INEFFECTIVE DRUG (Drug ineffective (10013709), Drug ineffective (10013709))
Unknown

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)

Cont..

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☑ NA

15. DAILY DOSE(S)

1) (22.5 milligram(s), 1 in 3 Month)

Cont..

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous

Cont..

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ NA

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) prostate cancer [10060862 - Prostate cancer]

Cont..

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION

III. CONCOMITANT DRUG(S) AND HISTORY

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

1)Chemotherapy(OTHER THERAPEUTIC PRODUCTS)

Cont..

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
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.-22DO036196
24c. DATE RECEIVED BY MANUFACTURER: 03/Apr/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 14/Apr/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...)

Event Description :

This study report from Dominican Republic was received by Adium ((reference number: (DO-0115-20220817) on 16-Aug-2022, from a consumer (patient's daughter) regarding an elderly-74 year old male patient who experienced a serious event of ‘stage 5 due to prostate cancer and with metastasis' (prostate cancer metastatic) during Eligard (leuprolide acetate) 22.5 mg therapy for prostate cancer. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 17-Aug-2025.

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

Concomitant medication included chemotherapy and unspecified injection.

On an unknown date, the patient began receiving Eligard 22.5 mg every 3 months via subcutaneous route for prostate cancer (Lot numbers and expiration dates were not reported). No further details were provided.

On an unknown date, the patient was in delicate health in stage 5 due to prostate cancer with metastasis. No further details were provided.

On 03-Apr-2022, the patient was prescribed with drug Xtandi indicating that he had never used it due to the shortage in the “Alto costo" establishment and that the delivery had not been authorized yet.

Corrective treatment was unknown.

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

The outcome of prostate cancer metastatic was not recovered/not resolved.

The reporter did not assess the seriousness of event prostate cancer metastatic.

The reporter did not provide the causality of prostate cancer metastatic in relation to Eligard and Eligard Unspecified Device.

On 03-Apr-2025, follow up information was received via by Adium ((reference number: (DO-0115-20220817) on 03-Apr-2025, from a consumer (patient's daughter). New information included: New information included: New serious event (medically significant) of ‘elevated PSA' (prostatic specific antigen increased) and non-serious event of 'ineffective drug' (drug ineffective) were added. Eligard 45 mg dose details were added. Treatment details were added. Relevant test results were added.

On 18-Aug-2022, the patient had an appointment, and he probably will change the dose to 45 mg, every 6 months via subcutaneous route for prostate cancer.

On 01-Sep-2022, the patient received Eligard 22.5 mg, every 3 months via subcutaneous route for prostate cancer.

On an unknown date, the patient daughter mentioned that the patient new oncologist switched him from Eligard to Bitara treatment takes 4 pills a day as the patient PSA was rising to 800ng/ml and with new treatment it was monitored that the patient PSA was dropped to 41ng/ml.

Corrective treatment included Bitara-takes 4 pills a day.

Relevant test results included:

On an unknown date: prostatic specific antigen increased: 800 ng/ml (Ref range: not provided)

On an unknown date: prostatic specific antigen increased: 40 ng/ml (Ref range: not provided)

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

The outcome of ineffective drug and prostatic specific antigen increased was unknown.

The reporter did not assess the seriousness of event ineffective drug and prostatic specific antigen increased.

The reporter did not provide the causality of ineffective drug and prostatic specific antigen increased in relationship to Eligard and Eligard Unspecified Device.

Listedness of the event Prostate cancer metastatic is retained as per previous assessment.

Continuation Sheet for CIOMS report

Prostatic specific antigen increased>Eligard>Listed as per CCDS>07-Nov-2024
Prostatic specific antigen increased>Eligard>Listed as per USPI>Feb-2025
Prostatic specific antigen increased>Eligard unspecified device>Listed as per USPI>Feb-2025
Prostatic specific antigen increased>Eligard>Listed as per Canadian monograph>02-Apr-2025

Drug ineffective >Eligard>Listed as per CCDS>07-Nov-2024
Drug ineffective>Eligard>Listed as per USPI>Feb-2025
Drug ineffective>Eligard unspecified device>Listed as per USPI>Feb-2025
Drug ineffective>Eligard>Listed as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (tolmar): This is 74 years old male patient who is experiencing stage 5 due to prostate cancer and with metastasis (Prostate cancer metastatic) during Eligard therapy (Leuprolide acetate) 22.5 mg for Prostate cancer. Tolmar assessed the event prostate cancer metastatic as serious (medically significant). Based on the information available and considering the inherent progressive nature of the underlying prostate the event prostate cancer metastatic is considered as not related to Eligard (drug and device) but considered as related to prostate cancer.

Follow-up: events drug ineffective (ineffective drug') and prostatic specific antigen increased (elevated PSA') during Eligard therapy (Leuprolide acetate) for Prostate cancer were added. Tolmar assessed the event prostatic specific antigen increased as serious (medically significant) and the event drug ineffective as non-serious since it did not meet ICH seriousness criteria. The causality of the events Drug ineffective and prostatic specific antigen increased was assessed as not related to Eligard drug (unrelated to device) but related to prostate metastatic cancer, considering the inherent progressive nature of the underlying prostate cancer.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
PSA		800 nanogram per millliiter	
PSA		40 nanogram per millliiter	

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
Form of Admin : 1) Injection
Daily Dose : (22.5 milligram(s), 1 in 3 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Drug withdrawn

Causality

1) STAGE 5 DUE TO PROSTATE CANCER AND WITH METASTASIS (Prostate cancer metastatic - 10036909, Prostate cancer metastatic - 10036909)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) ELEVATED PSA (Prostatic specific antigen increased - 10036975, Prostatic specific antigen increased - 10036975)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) INEFFECTIVE DRUG (Drug ineffective - 10013709, Drug ineffective - 10013709)
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) STAGE 5 DUE TO PROSTATE CANCER AND WITH METASTASIS
CORE Labeled
2) ELEVATED PSA
CORE Labeled
3) INEFFECTIVE DRUG
CORE Labeled

2) Drug : Eligard 45 mg (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form of Admin : 1) Injection
Daily Dose : (45 milligram(s), 1 in 6 Month)
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Unknown

Causality

1) STAGE 5 DUE TO PROSTATE CANCER AND WITH METASTASIS (Prostate cancer metastatic - 10036909, Prostate cancer metastatic - 10036909)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) ELEVATED PSA (Prostatic specific antigen increased - 10036975, Prostatic specific antigen increased - 10036975)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) INEFFECTIVE DRUG (Drug ineffective - 10013709, Drug ineffective - 10013709)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) STAGE 5 DUE TO PROSTATE CANCER AND WITH METASTASIS
CORE Labeled
2) ELEVATED PSA
CORE Labeled
3) INEFFECTIVE DRUG
CORE Labeled

3) 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) STAGE 5 DUE TO PROSTATE CANCER AND WITH METASTASIS (Prostate cancer metastatic - 10036909, Prostate cancer metastatic - 10036909)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) ELEVATED PSA (Prostatic specific antigen increased - 10036975, Prostatic specific antigen increased - 10036975)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) INEFFECTIVE DRUG (Drug ineffective - 10013709, Drug ineffective - 10013709)
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) STAGE 5 DUE TO PROSTATE CANCER AND WITH METASTASIS
   CORE
2) ELEVATED PSA
   CORE
3) INEFFECTIVE DRUG
   CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 milligram, q 3 month

Drug 3 :Eligard® Unspecified Device

1) UNK

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

1). Drug	:	Chemotherapy
Active Substance	:	1) OTHER THERAPEUTIC PRODUCTS
Form Strength	:	
Indications	:	1) Product used for unknown indication [10070592 - Product used for unknown indication]

2). Drug	:	Injection
Active Substance	:	1) OTHER THERAPEUTIC PRODUCTS
Form Strength	:	
Indications	:	1) Product used for unknown indication [10070592 - Product used for unknown indication]