CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

DO-TOLMAR, INC.-25DO056861

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	
MARR	DOMINICAN Cont..	18	Nov	1964	60	Male			2025	

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

1) Increased liver level/Elevated Liver Enzymes three times the normal value (Hepatic enzyme increased (10060795), Hepatic enzyme increased (10060795))
(//2025 -) - Recovering/Resolving
2) Experiencing flu (Flu (10016790), Influenza (10022000))
(11/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing
3) Mucous discharge (Mucous discharge (10073764), Secretion discharge (10053459))
(11/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing
4) Overall body aches (General body pain (10048971), Pain (10033371))
(11/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing

Cont..

- ☐ 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) (Injection)(5109CUY; UNK; UNK)

Cont..

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

15. DAILY DOSE(S)

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

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ 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) (10/Nov/2023 - Ongoing)	

III. CONCOMITANT DRUG(S) AND HISTORY

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

1)VITAMINE C(ASCORBIC ACID)

Cont..

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

1) PROSTATE CANCER (10060862, Prostate cancer) (//2023 -) (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

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.-25DO056861
24c. DATE RECEIVED BY MANUFACTURER: 22/May/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 04/Jun/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) Secretion (Nasal discharge (10028737), Rhinorrhoea (10039101)(11/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

6) JOINT PAIN (Joint pain (10023222), Arthralgia (10003239)(11/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

7) MUSCLE PAIN (Muscle pain (10028322), Myalgia (10028411)(11/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from DOMINICAN REPUBLIC was received by Adium via Asofarma a tu lado Patient Support Program (reference number: DO-ADIUM-DO-0011-20250212) on 12-FEB-2025 from a Consumer/Other Non-Health Prof regarding an Adult 60 Years old Male patient who experienced flu (Flu), Hepatic enzyme increased (Hepatic enzyme increased), Mucous discharge (Mucous discharge), Overall body aches (General body pain), Secretion (Nasal discharge), Joint pain (Joint pain), Muscle pain (Muscle pain), 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 17-FEB-2025.

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

Concomitant medications included Vitamin C, High-dose intravenous vitamin C, homemade cinnamon tea and homemade ginger tea.

On 08-NOV-2023, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for Prostate cancer (Lot numbers and Expiration dates not provided).

On 11-FEB-2025, unknown time after the most recent dose of Eligard, the patient experienced flu, presenting with mucus (mucous discharge), secretion, joint pain, and muscle pain, referring to overall body aches. Also, his liver levels, as shown in laboratory tests (no further details provided), had increased. However, according to his urologist, this was caused by Eligard, not a cause for concern. Corrective treatment was not reported. Action taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were Not applicable. The outcome of Hepatic enzyme increased was Unknown. The outcome of Flu, Mucous discharge, General body pain, Nasal discharge, Joint pain and Muscle pain was Not Recovered/Not Resolved.

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

On 22-May-2025, the follow up information was received by Adium via Asofarma a tu lado Patient Support Program (reference number: DO-ADIUM-DO-0011-20250212) from a consumer (non-healthcare professional) and sent to Tolmar on 23-May-2025. New information included: added confirmed start date, lot number and expiration date of Eligard and new lab test. Updated verbatim of 'Hepatic enzyme increased' from 'Increased liver level' to 'Increased liver level/Elevated Liver Enzymes three times the normal value' and outcome from "unknown" to "resolving" along with treatment drug. Updated seriousness criteria of the event Hepatic enzyme increased from "non-serious" to "serious" (medically significant). Narrative was updated. The case was upgraded from non-serious to serious.

On 10-Nov-2023, the patient began receiving Eligard 22.5 mg, every 3 months via subcutaneous route for prostate cancer (Lot numbers: 5109CUY; UNK; UNK and Expiration dates: Mar-2026; UNK; UNK).

On an unknown date in 2025, the patient experienced elevated liver enzymes three times the normal value, requiring treatment with N-acetylcysteine. He said that they had decreased since starting the treatment, although they were still not within normal limits. No further details were provided.

Corrective treatment included N-acetylcysteine (acetylcysteine).

Relevant test results included:
On an unknown date: Hepatic enzyme increased: elevated three times the normal value (Ref. range: Not provided).

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

The outcome of hepatic enzyme increased was resolving.

The reporter assessed the seriousness of hepatic enzyme increased as non-serious.

The reporter assessed the causality of the hepatic enzyme increased in relationship to Eligard and Eligard unspecified device as not related.

No further information is expected as consent to be contacted was not provided.

Listedness of the events Influenza, hepatic enzyme increased, secretion discharge, pain, rhinorrhoea, arthralgia, and myalgia is retained as per previous assessment.

Company Remarks (Sender's Comments) :

Continuation Sheet for CIOMS report

Evaluator comment (Tolmar):
Hepatic enzyme increased-Related to Drug and not related to device
Influenza-Not related to drug and device
Secretion discharge-Not related to drug and device
Pain-Not related to drug and device
Rhinorrhoea-Not related to drug and device
Arthralgia-related to drug and not related to device
Myalgia-Not related to drug and not related to device

Causality of the events Influenza, hepatic enzyme increased, secretion discharge, pain, rhinorrhoea, arthralgia, and myalgia is retained as per previous assessment.

FU added event of hepatic enzyme increased- The causality of event hepatic enzyme increased was assessed as serious (medically significant) based on medical judgment that the liver enzymes were increased to three times the normal value, requiring treatment with N-acetylcysteine (medical intervention). Considering the close temporality, role of drug component of Eligard cannot be ruled out with the event hepatic enzyme increased. The event hepatic enzyme increased was assessed as not related to device component of Eligard.

Additional Information (Continuation...)

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

1) Test Name: HEPATIC ENZYME INCREASED

Result Unstructured Data (free text) : Increased
Test Date:

2) Test Name: HEPATIC ENZYME INCREASED

Result Unstructured Data (free text) : elevated three times the normal value
Test Date:

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
Lot Number	: 1) 5109CUY; UNK; UNK
Daily Dose	: (22.5 milligram(s), 1 in 3 Month)
Route of Admin	: 1) Subcutaneous
Indications	: 1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	: 1) From : 10/Nov/2023 To :Continuing
Action(s) Taken With Drug	: Dose not changed

Causality

1) Increased liver level/Elevated Liver Enzymes three times the normal value (Hepatic enzyme increased - 10060795, Hepatic enzyme increased - 10060795)

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

2) Experiencing flu (Flu - 10016790, Influenza - 10022000)

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

3) Mucous discharge (Mucous discharge - 10073764, Secretion discharge - 10053459)

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

4) Overall body aches (General body pain - 10048971, Pain - 10033371)

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

Continuation Sheet for CIOMS report

5) Secretion (Nasal discharge - 10028737, Rhinorrhoea - 10039101)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
6) JOINT PAIN (Joint pain - 10023222, Arthralgia - 10003239)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
7) MUSCLE PAIN (Muscle pain - 10028322, Myalgia - 10028411)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Increased liver level/Elevated Liver Enzymes three times the normal value
CORE UnLabeled
2) Experiencing flu
CORE UnLabeled
3) Mucous discharge
CORE UnLabeled
4) Overall body aches
CORE UnLabeled
5) Secretion
CORE Labeled
6) JOINT PAIN
CORE Labeled
7) MUSCLE PAIN
CORE Labeled

2) Drug : Eligard® Unspecified Device (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form of Admin : 1) Injection
Lot Number : 1) 5109CUY; UNK; UNK
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Action(s) Taken With Drug : Not applicable

Causality

1) Increased liver level/Elevated Liver Enzymes three times the normal value (Hepatic enzyme increased - 10060795, Hepatic enzyme increased - 10060795)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Experiencing flu (Flu - 10016790, Influenza - 10022000)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) Mucous discharge (Mucous discharge - 10073764, Secretion discharge - 10053459)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) Overall body aches (General body pain - 10048971, Pain - 10033371)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
5) Secretion (Nasal discharge - 10028737, Rhinorrhoea - 10039101)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Continuation Sheet for CIOMS report

6) JOINT PAIN (Joint pain - 10023222, Arthralgia - 10003239)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) MUSCLE PAIN (Muscle pain - 10028322, Myalgia - 10028411)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Increased liver level/Elevated Liver Enzymes three times the normal value
CORE
2) Experiencing flu
CORE
3) Mucous discharge
CORE
4) Overall body aches
CORE
5) Secretion
CORE
6) JOINT PAIN
CORE
7) MUSCLE PAIN
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) Expiration Date-Mar-2026; UNK; UNK

Drug 2 :Eligard® Unspecified Device

1) Expiration Date-Mar-2026; UNK; UNK

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

1). Drug : VITAMINE C
Active Substance : 1) ASCORBIC ACID
Form Strength :
Daily Dose : 1) (1 in 1 Day)
Route of Admin : 1) Oral
Indications : 1) To prevent the flu [10049087 - Antiviral prophylaxis]

2). Drug : VITAMINE C
Active Substance : 1) ASCORBIC ACID
Form Strength :
Daily Dose : 1) (1 in 3 Month)
Route of Admin : 1) Intravenous (not otherwise specified)
Indications : 1) To prevent the flu [10049087 - Antiviral prophylaxis]

3). Drug : CINNAMON [NEOLITSEA CASSIA]
Active Substance : 1) NEOLITSEA CASSIA
Form Strength :
Route of Admin : 1) Oral
Indications : 1) Drug use for unknown indication [10070592 - Product used for unknown indication]

4). Drug : GINGER ROOT EXTRACT
Active Substance : 1) ZINGIBER OFFICINALE ROOT
Form Strength :
Route of Admin : 1) Oral
Indications : 1) Drug use for unknown indication [10070592 - Product used for unknown indication]

Continuation Sheet for CIOMS report