SUSPECT ADVERSE REACTION REPORT

TLM-2025-01456 (0), GT-TOLMAR, INC.-24GT053806

## 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 |
| JGLZ | GUATEMALA | 19 | Apr | 1956 | 68 | Male | 29 | Oct | 2024 |

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

1) PAIN ON THE RIGHT SIDE OF THE FACE (Facial pain (10016059), Facial pain (10016059))
(29/Oct/2024 - ) - Not Recovered/Not Resolved/Ongoing
2) COLD SENSATION (Feeling cold (10016326), Feeling cold (10016326))
(30/Oct/2024 - ) - Not Recovered/Not Resolved/Ongoing
3) Lung pain (Lung pain (10083482), Pulmonary pain (10074693))
(/Mar/2025 - ) - Not Recovered/Not Resolved/Ongoing
4) Pain throughout the body (General body pain (10048971), Pain (10033371))
(/Mar/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) (Injection)(Unknown)(Unknown)

Cont..

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

| 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 |

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

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Prostatic cancer [10036946 - Prostatic cancer]

| 18. THERAPY DATE(S) (from/to) | 19. THERAPY DURATION |
|---|---|
| 1) (30/Nov/2023 - Ongoing) | |

## III. CONCOMITANT DRUG(S) AND HISTORY

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

1)ACID 200(CIPROFLOXACIN HYDROCHLORIDE)

Cont..

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

1) DRAINAGE IN RIGHT LUNG (10084562, Drainage) (22/May/2023 - ) (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

Study Information
Study Name: NA
EudraCT Number:
Protocol No.: NA
Center No.:
Subject Id :

| 24.REPORT NULLIFIED | 24b. MFR CONTROL NO. |
|---|---|
| ☐ YES ☐ NO | TLM-2025-01456 (0), GT-TOLMAR, |
| 24c. DATE RECEIVED BY MANUFACTURER: 05/May/2025 | 24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL |
| DATE OF THIS REPORT: 16/May/2025 | 25a. REPORT TYPE: ☑ INITIAL ☐ FOLLOWUP |

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) SEVERE PAIN IN ONE LEG, FROM THE WAIST DOWN (Leg pain (10024130), Pain in extremity (10033425) - Unknown)

6) GENERAL MALAISE (General malaise (10018066), Malaise (10025482)(30/Oct/2024 - ) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from GUATEMALA was received by Adium (reference number: GT-ADIUM-GT-0507-20241030) on 30-OCT-2024 from a Consumer/ Other Non-Health Prof regarding an Elderly 68-Year-old male patient who experienced Pain on the right side of the face, cold sensation and General malaise (Facial pain), (Feeling cold), (General malaise) during Eligard (Leuprolide acetate) 22.5 milligram therapy for Prostatic cancer. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 31-OCT-2024.

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

Concomitant medications were not reported.

On 23-OCT-2023, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for Prostatic cancer (Lot number and expiration date details were not provided).

On 29-OCT-2024, 1 year 7 days after the most recent dose of Eligard, the patient experienced pain on the right side of the face and took a neurobion but it gave little relief.

On 30-OCT-2024, felt a lot of pain.

On 30-OCT-2024, 1 year 8 days after the most recent dose of Eligard, the patient experienced cold sensation and general malaise.

Corrective treatment included neurobion for facial pain.

Action taken with Eligard treatment in response to the events were dose not changed, de-challenge and re-challenge were not applicable.

The outcome of Facial pain was Not Recovered/Not Resolved. The outcome of Feeling cold was Not Recovered/Not Resolved.

The outcome of General malaise was Not Recovered/Not Resolved.

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

On 06-FEB-2025, follow-up information was received by Adium (reference number: GT-ADIUM-GT-0507-20241030) from a Consumer/Other Non-Health Prof and sent to Tolmar on 07-FEB-2025.

New information included addition of non-serious events of significant pain all over his body (General body pain) and severe pain in one leg, from the waist down (Leg pain), new reporter, medical history, concomitant medication, treatment medication, most recent dose of Eligard, update to first dose date of Eligard and updated event verbatim to General malaise/patient became unwell.

The patient's medical history and current conditions included lung neoplasm malignant, drainage, and biopsy skin.

Concomitant medications included Acid (ciprofloxacin hydrochloride).

On 30-NOV-2023, the patient began receiving Eligard 22.5 milligram, q 3 month via subcutaneous use for prostatic cancer (Lot number and expiration date: not reported).

On unspecified date about 1 month ago, the patient became unwell because patient was experiencing significant pain all over his body and this pain had intensified even more because an acid was applied to the patient for his bones which was administered every 3 months, and therefore the pain continued to the present.

On unspecified date last Sunday, the patient experienced severe pain in one leg, from the waist down, and as a result, the patient was taken to a clinic where the doctor indicated that if the pain was too severe, patient would not take the medication previously prescribed (Dolgenal) because patient would need a stronger medication.

On 26-JAN-2025, patient was given a dose of morphine, and it was the only dose administered to the patient.

On 30-JAN-2025, the patient received Eligard 22.5 milligram, q 3 month via subcutaneous use (Lot number and expiration date: not reported).

Corrective treatment included Dolgenal [ketorolac tromethamine] and Tramal with tylenol (paracetamol, tramadol hydrochloride) both for body pain, and Morfina [morphine] for severe pain in one leg, from the waist down.

Action taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were not applicable.

Continuation Sheet for CIOMS report

The outcome of general body pain was Not Recovered/Not Resolved.

The outcome of general malaise was Not Recovered/Not Resolved. The outcome of leg pain was Unknown.

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

On 05-May-2025, follow up information was received by Adium via the PSP Solutions (Patient Support Program) (ASOFARMA A TU LADO) (reference number: GT-ADIUM-GT-0507-20241030), from a consumer. New information included: Updated clinical details of previously reported event of (pain) and added a new non-serious event of ' lung pain' (Pulmonary pain). Updated event verbatim for event malaise. The report was sent to Tolmar on 06-May-2025.

On an unknown date in Mar-2025, the patient experienced body and lung pain. No further information was available.

Corrective treatment was not reported.

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

The outcome of pulmonary pain and pain was not recovered.

The reporter did not assess the seriousness of pulmonary pain and pain.

The reporter did not provide the causality of pulmonary pain and pain in relationship to Eligard and Eligard unspecified device.

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

Listedness of events facial pain, pain, pain in extremity, feeling cold and malaise retained as per previous assessment.
Pulmonary pain>Eligard>Unlisted as per CCDS>07-Nov-2024
Pulmonary pain>Eligard>Unlisted as per USPI>Feb-2025
Pulmonary pain>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Pulmonary pain>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar):
Causality of the previously reported events retained as per previous assessment:
Facial pain: Not related to drug and device.
Pain: Not related to drug and device.
Pain in extremity: Related to drug and not related to device.
Feeling cold: Not related to drug and device.
Malaise: Not related to drug and device.
On receipt of follow up information, regarding a patient who had pulmonary pain (lung pain) during Eligard (leuprolide acetate) 22.5 mg therapy for prostate cancer. Tolmar assessed the reported event as non-serious since it did not meet the ICH seriousness criteria and is not IME event. Event pulmonary pain was assessed as not related to Eligard (Drug and device) as the event can be explained by underlying medical history of lung neoplasm malignant.

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 |
| | | 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) Prostatic cancer [10036946 - Prostatic cancer] |
| Therapy Dates | : | 1) From : 30/Nov/2023 To :Continuing |
| | | 2) From : 30/Jan/2025 To :Continuing |
| Action(s) Taken With Drug | : | Dose not changed |

Continuation Sheet for CIOMS report

Causality

1) PAIN ON THE RIGHT SIDE OF THE FACE (Facial pain - 10016059, Facial pain - 10016059 )
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

2) COLD SENSATION (Feeling cold - 10016326, Feeling cold - 10016326 )
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

3) Lung pain (Lung pain - 10083482, Pulmonary pain - 10074693 )
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

4) Pain throughout the body (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) SEVERE PAIN IN ONE LEG, FROM THE WAIST DOWN (Leg pain - 10024130, Pain in extremity - 10033425 )
- Causality as per reporter : Not Reported
- Causality as per Mfr : Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

6) GENERAL MALAISE (General malaise - 10018066, Malaise - 10025482 )
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

Labeling :

1) PAIN ON THE RIGHT SIDE OF THE FACE
- CORE UnLabeled

2) COLD SENSATION
- CORE UnLabeled

3) Lung pain
- CORE UnLabeled

4) Pain throughout the body
- CORE Labeled

5) SEVERE PAIN IN ONE LEG, FROM THE WAIST DOWN
- CORE Labeled

6) GENERAL MALAISE
- 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) Unknown
- Indications : 1) Prostatic cancer [10036946 - Prostatic cancer]
- Action(s) Taken With Drug : Not applicable

Causality

1) PAIN ON THE RIGHT SIDE OF THE FACE (Facial pain - 10016059, Facial pain - 10016059 )
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

2) COLD SENSATION (Feeling cold - 10016326, Feeling cold - 10016326 )
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

3) Lung pain (Lung pain - 10083482, Pulmonary pain - 10074693 )

Continuation Sheet for CIOMS report

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

4) Pain throughout the body (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) SEVERE PAIN IN ONE LEG, FROM THE WAIST DOWN (Leg pain - 10024130, Pain in extremity - 10033425 )
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) GENERAL MALAISE (General malaise - 10018066, Malaise - 10025482 )
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) PAIN ON THE RIGHT SIDE OF THE FACE
CORE
2) COLD SENSATION
CORE
3) Lung pain
CORE
4) Pain throughout the body
CORE
5) SEVERE PAIN IN ONE LEG, FROM THE WAIST DOWN
CORE
6) GENERAL MALAISE
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 : ACID 200
Active Substance : 1) CIPROFLOXACIN HYDROCHLORIDE
Form Strength :
Daily Dose : 1) ( in 3 Month)
Indications : 1) for his bones [10005956 - Bone disorder]

23. OTHER RELEVANT HISTORY (Continuation...)

2) RIGHT LUNG SCRAPING (10004873 , Biopsy skin) (23/Aug/2023 - ) (Continuing : NO )

3) RIGHT LUNG CANCER (10025044 , Lung cancer) (07/Sep/2023 - ) (Continuing : YES )

4) PROSTATIC CANCER (10036946 , Prostatic cancer) (Continuing : YES )