SUSPECT ADVERSE REACTION REPORT

NI-TOLMAR, INC.-25NI055661

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
KDAT	NICARAGUA	02	Dec	2016	8	Female		Nov	2024

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

1) BREAST GROWTH (Breast enlargement female (10006243), Breast enlargement (10006242))
(/Nov/2024 -) - Not Recovered/Not Resolved/Ongoing
2) SHORTENED FREQUENCY FROM 24 TO 22 WEEKS (Off label dosing frequency (10076395), Off label use (10053762))
Unknown
3) Increase of 13 pounds (Weight gain (10047896), Weight increased (10047899))
(/Jan/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) (45, Injection)(Unknown)

Cont..

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

15. DAILY DOSE(S)

1) (45 milligram(s), 1 in 6 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) Central Precocious Puberty [10073186 - Central precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (01/Mar/2024 - Ongoing)	

III. CONCOMITANT DRUG(S) AND HISTORY

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

No concomitants used/reported

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

1) CENTRAL PRECOCIOUS PUBERTY (10073186, Central precocious puberty) (Asked but Unknown -) (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
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	NI-TOLMAR, INC.-25NI055661
24c. DATE RECEIVED BY MANUFACTURER: 06/Jun/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 17/Jun/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...)

Event Description :

This Study report from NICARAGUA was received by Adium via "Asofarma a tu lado" Patient support program (reference number: NI-ADIUM-NI-0005-20250110) on 10-JAN-2025 from a Consumer/Other Non-Health Prof regarding an Child 8 Years old Female patient who experienced Breast growth (Breast enlargement female) and Shortened frequency from 24 to 22 weeks (Off label dosing frequency) during Eligard (Leuprolide acetate) 45 milligram therapy for Central precocious puberty. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 13-JAN-2025.

The patient's medical history and current conditions included precocious puberty.

Concomitant medications were not reported.

On 01-MAR-2024, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Central precocious puberty (Lot numbers and expiration dates were not reported).

In NOV-2024, after an unspecified amount of time from most recent dose of Eligard, the patient experienced breast growth.

On 28-DEC-2024, she had an appointment with an endocrinologist who, upon physical examination, corroborated the increase and reviewed unspecified laboratory tests which showed that she was not blocked. Due to this, the doctor shortened the time of application of Eligard 45 milligram, from 24 to 22 weeks.

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

The outcome of Breast enlargement female was Not Recovered. The outcome of Off label dosing frequency was Unknown.

Relevant test results included:

Unknown date: Laboratory test: showed the patient was not blocked.

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

On 06-Jun-2025, follow up information was received by Adium via patient Support Program ‘ASOFARMA A TU LADO' (reference number: (NI-ADIUM-NI-0005-2025011 (1)), from a consumer and sent to Tolmar on 07-Jun-2025. New information included: New non-serious event of ‘increase of 13 pounds' (weight increased) was added. Relevant test results were added. Narrative was updated.

On an unknown date in Jan-2025, the patient had gained 13 pounds of weight. No further details were provided.

Corrective treatment included diet.

Relevant test results included:
On an unknown date: Weight: 13-pound weight gain (Ref. range: Not provided).

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

The outcome of weight increased was not resolved.

The reporter did not assess the seriousness of weight increased.

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

No further queries were raised.

Listedness of events breast enlargement and off label use retained as per previous assessment.
Weight increased>Eligard>listed as per CCDS>07-Nov-2024
Weight increased>Eligard>listed as per USPI>Feb-2025
Weight increased>Eligard unspecified device>listed as per USPI>Feb-2025
Weight increased>Eligard>listed as per Canadian monograph>O2-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar):
Causality of previously reported events retained as per previous assessment:
Breast enlargement: Related to drug and not related to device.
Off label use: Not related to drug and device.

Continuation Sheet for CIOMS report

On receipt of follow up information, regarding a child 08-year-old female patient who had weight increased (Increase of 13 pounds) during Eligard (leuprolide acetate) 45 mg therapy for precocious puberty. Tolmar assessed the reported event as non-serious since it did not meet the ICH seriousness criteria and is not IME event. The event weight increased was assessed as related as the contributory role of suspect drug Eligard cannot be ruled out considering known pharmacological profile of the drug. Weight increased was assessed as not related to the device component of Eligard.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
LABORATORY TEST	Unknown		
WEIGHT	Unknown		

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

1) Test Name: LABORATORY TEST

Result Unstructured Data (free text) : showed that
she was not blocked

Test Date: Unknown

2) Test Name: WEIGHT

Result Unstructured Data (free text) : 13-pound weight gain

Test Date: Unknown

Lab Comments :

1) Test Name : LABORATORY TEST

Lab Comments : showed that she was not blocked

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

Product-Reaction Level

1) Drug : Eligard® (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form Strength : 1) 45
Form of Admin : 1) Injection
Lot Number : 1) Unknown
Daily Dose : (45 milligram(s), 1 in 6 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) Central Precocious Puberty [10073186 - Central precocious puberty]
Therapy Dates : 1) From : 01/Mar/2024 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) BREAST GROWTH (Breast enlargement female - 10006243, Breast enlargement - 10006242)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) SHORTENED FREQUENCY FROM 24 TO 22 WEEKS (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

3) Increase of 13 pounds (Weight gain - 10047896, Weight increased - 10047899)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) BREAST GROWTH
CORE Labeled

Continuation Sheet for CIOMS report

2) SHORTENED FREQUENCY FROM 24 TO 22 WEEKS
CORE UnLabeled
3) Increase of 13 pounds
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
Route of Admin : 1) Subcutaneous
Indications : 1) Central Precocious Puberty [10073186 - Central precocious puberty]
Action(s) Taken With Drug : Not applicable

Causality

1) BREAST GROWTH (Breast enlargement female - 10006243, Breast enlargement - 10006242)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) SHORTENED FREQUENCY FROM 24 TO 22 WEEKS (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
3) Increase of 13 pounds (Weight gain - 10047896, Weight increased - 10047899)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) BREAST GROWTH
CORE
2) SHORTENED FREQUENCY FROM 24 TO 22 WEEKS
CORE
3) Increase of 13 pounds
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

Drug 2 :Eligard® Unspecified Device

1) 45 milligram, q 6 month