SUSPECT ADVERSE REACTION REPORT

NI-TOLMAR, INC.-24NI046251

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
GERM	NICARAGUA	17	Aug	2015	8	Female	29	Sep	2023

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

1) Patient was using Eligard 22.5 mg for central precocious puberty (Off label use (10053762), Off label use (10053762)) (29/Sep/2023 -) - Unknown
2) Sudden mood swings (Mood swings (10027951), Mood swings (10027951)) (12/Oct/2023 -) - Not Recovered/Not Resolved/Ongoing
3) Increased irritability to the environment (Irritability (10022998), Irritability (10022998)) (12/Oct/2023 -) - Not Recovered/Not Resolved/Ongoing
4) Suspension due to improvement (Therapy cessation (10065154), Therapy cessation (10065154)) (/May/2025 -) - 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)(Unknown)

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) Central precocious puberty [10073186 - Central precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (29/Sep/2023 - /May/2025)	

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.-24NI046251
24c. DATE RECEIVED BY MANUFACTURER: 27/Jun/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 08/Jul/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) Weight gain (Weight gain (10047896), Weight increased (10047899)(/Aug/2024 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from NICARAGUA was received by Adium (reference number: NI-ADIUM-NI-0003-20240117) on 17-JAN-2024 from a Consumer regarding a Child 8 Years old Female patient who experienced Sudden mood swings (Mood swings), Increased irritability to the environment (Irritability), during Eligard (Leuprolide acetate) 22.5 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 18-JAN-2024.

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

Concomitant medications were not reported.

On 29-SEP-2023, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for Central precocious puberty (Lot numbers and Expiration dates were not provided). On 12-OCT-2023, 14 days after the most recent dose of Eligard, the patient started having sudden mood swings (altered mood) and increased irritability to the environment (irritability). No further details were provided.

Corrective treatment was not reported.

Action taken with Eligard in response to the event(s) was Dose Not Changed. De-challenge was not applicable, and re-challenge was not applicable.

The outcome of Mood swings was Not Recovered. The outcome of Irritability was Not Recovered.

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

On 10-JAN-2025, follow-up information was received by Adium via patient support program (reference number: NI-ADIUM-NI-0003-20240117) from a Consumer/Other Non-Health Prof and sent to Tolmar on 13-JAN-2025. New information included: Added new non serious event of Weight gain (Weight gain) and respective laboratory.

On an unspecified date in AUG-2024, at an unknown amount of time after the most recent dose of Eligard, the patient gained weight.

Since AUG-2024 to JAN-2025 she gained 3 kilograms (kg).

Corrective treatment was not reported.

Relevant test results included:
AUG-2024: Weight: Gained 3 kilograms (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 gain was Not Recovered.

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

On 27-Jun-2025, follow-up information was received by Adium via Patient Support Program “Asofarma a tu Lado” (reference number: NI-ADIUM-NI-0003-2024011) from a consumer (non-healthcare professional) and sent to Tolmar on 28-Jun-2025. New information included: added two new non-serious events of "Suspension for improvement" (Therapy cessation) and "Patient was using Eligard 22.5 mg for central precocious puberty" (Off label use).

On an unknown date in May-2025, patient suspended the Eligard therapy due to improvement.

Corrective treatment was not reported.

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

The outcome of therapy cessation and Off label use was Unknown.

The reporter did not assess the seriousness of therapy cessation and off label use.

The reporter assessed the causality of therapy cessation in relationship to Eligard and Eligard unspecified device as not related and did not provide the causality of off label use.

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

Listedness
Listedness of the events mood swings, irritability and weight gain is retained as per previous assessment.

Continuation Sheet for CIOMS report

Off label use>Eligard>Unlisted as per CCDS>07-Nov-2024
Off label use>Eligard>Unlisted as per USPI>Feb-2025
Off label use>Eligard unspecified device>Unisted as per USPI>Feb-2025
Off label use>Eligard>Unisted as per Canadian monograph>02-Apr-2025

Therapy cessation>Eligard>Unlisted as per CCDS>07-Nov-2024
Therapy cessation>Eligard>Unlisted as per USPI>Feb-2025
Therapy cessation>Eligard unspecified device>Unisted as per USPI>Feb-2025
Therapy cessation>Eligard>Unisted as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): Causality
Mood swings-Not related to drug and device
Irritability -Not related to drug and device
Weight gain-Related to drug and not related to device

FU- Events Off label use ("Patient was using Eligard 22.5 mg for central precocious puberty") and therapy cessation ("Suspension for improvement") were added. Tolmar assessed the event as non-serious since it does not meet the ICH seriousness criteria and is not an IME event. The reported events were assessed as not related to Eligard (drug and device) as the event occurred with the product due to human action, rather due to the drug. Causality of the events mood swings, irritability and weight gain is retained as per previous assessment.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
WEIGHT GAIN	/Aug/2024		

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

1) Test Name: WEIGHT GAIN

Result Unstructured Data (free text) : Notes: Gained 3 Kilograms
Test Date: /Aug/2024

Lab Comments :

1) Test Name : WEIGHT GAIN
Lab Comments : Gained 3 Kilograms

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
Lot Number : 1) Unknown
Daily Dose : (22.5 milligram(s), 1 in 3 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) Central precocious puberty [10073186 - Central precocious puberty]
Therapy Dates : 1) From : 29/Sep/2023 To :/May/2025
Action(s) Taken With Drug : Unknown

Causality

1) Patient was using Eligard 22.5 mg for central precocious puberty (Off label use - 10053762, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Sudden mood swings (Mood swings - 10027951, Mood swings - 10027951)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related

Continuation Sheet for CIOMS report

DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Increased irritability to the environment (Irritability - 10022998, Irritability - 10022998)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Suspension due to improvement (Therapy cessation - 10065154, Therapy cessation - 10065154)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) Weight gain (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) Patient was using Eligard 22.5 mg for central precocious puberty
CORE UnLabeled
2) Sudden mood swings
CORE UnLabeled
3) Increased irritability to the environment
CORE UnLabeled
4) Suspension due to improvement
CORE UnLabeled
5) Weight gain
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) Patient was using Eligard 22.5 mg for central precocious puberty (Off label use - 10053762, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Sudden mood swings (Mood swings - 10027951, Mood swings - 10027951)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Increased irritability to the environment (Irritability - 10022998, Irritability - 10022998)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Suspension due to improvement (Therapy cessation - 10065154, Therapy cessation - 10065154)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) Weight gain (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 :

Continuation Sheet for CIOMS report

1) Patient was using Eligard 22.5 mg for central precocious puberty
   CORE
2) Sudden mood swings
   CORE
3) Increased irritability to the environment
   CORE
4) Suspension due to improvement
   CORE
5) Weight gain
   CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 milligram, q 3 month

Drug 2 :Eligard® Unspecified Device

1) UNK