SUSPECT ADVERSE REACTION REPORT

NI-TOLMAR, INC.-25NI057384

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
MACM	NICARAGUA	17	Oct	2016	7	Female	12	May	2024

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

1) Patient was using Eligard 22.5 mg for Central Precocious Puberty (Off label dosing (10074165), Off label use (10053762))
(12/May/2024 -) - Unknown
2) Sneezing (Sneezing (10041232), Sneezing (10041232))
(21/Dec/2024 - 21/Dec/2024) - Recovered/Resolved
3) Transparent mucus (Rhinorrhoea (10039101), Rhinorrhoea (10039101))
(21/Dec/2024 - 21/Dec/2024) - Recovered/Resolved
4) Brown vaginal discharge (Vaginal discharge (10046901), Vaginal discharge (10046901))
(23/Dec/2024 - 25/Dec/2024) - Recovered/Resolved

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
(05-Dec-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) (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	NI-TOLMAR, INC.-25NI057384
24c. DATE RECEIVED BY MANUFACTURER: 05/Jun/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 16/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...)

5) Increased appetite (Increased appetite (10021654), Increased appetite (10021654)(/May/2025 -) - Not Recovered/Not Resolved/Ongoing)

6) Weight gain (Weight gain (10047896), Weight increased (10047899)(/May/2025 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from NICARAGUA was received by Adium via patient support program (reference number: NI-ADIUM-NI-0026-20250305) on 05-MAR-2025 from a Consumer/Other Non-Health Prof regarding 8 Years old Female Child patient who experienced non serious events "Sneezing" (Sneezing), "Transparent mucus" (Rhinorrhoea), and "Brown vaginal discharge" (Vaginal discharge) 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 06-MAR-2025.

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

Concomitant medications were not reported.

On 05-DEC-2024, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use (in source reported as subconjunctival) for Central precocious puberty (Lot numbers and Expiration dates were not provided).

On 21-DEC-2024, 17 days after the most recent dose of Eligard, the patient experienced sneezing and clear mucus, but it only lasted for the same day.

On 23-DEC-2024, 19 days after the most recent dose of Eligard, the patient experienced brown vaginal discharge that lasted for two days (until 25-DEC-2024).

Corrective treatment was not reported.

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

The outcome of Sneezing was Recovered. The outcome of Rhinorrhoea was Recovered. The outcome of Vaginal discharge was Recovered.

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

On 05-Jun-2025, follow-up information was received from NICARAGUA via an electronic form through the Jazz Safety tool of the Patient Support Program “ASOFARMA A TU LADO" (Reference number: NI-ADIUM-NI-0026-20250305) from a Consumer/Other Non-Healthcare Professional and sent to Tolmar on 05-Jun-2025. New information included: Added new events "Increased appetite" (Increased appetite), "Weight gain" (Weight gain) and "Patient was using Eligard 22.5 mg for Central Precocious Puberty" (Off label use), lab data (Weight) and narrative was updated.

On an unknown date in May-2025, the patient had increased appetite (increased appetite) and weight gain (weight increased).

Corrective treatment was not reported.

Lab data included:
On an unknown date in May-2025: Weight gain; Reference range not provided.

Action taken with Eligard in response to the events increased appetite, weight increased and off label use was dose not changed. De-challenge and re-challenge were not applicable.

The outcome of the events increased appetite, weight increased and off label use was not resolved.

The reporter did not assess the seriousness of the events increased appetite, weight increased and off label use and assessed causality as related with increased appetite, weight increased in relationship to Eligard and Eligard unspecified device.

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

Rhinorrhoea >Eligard>listed as per CCDS>07-Nov-2024
Rhinorrhoea >Eligard>Unlisted as per USPI>Feb-2025
Rhinorrhoea >Eligard unspecified device>Unlisted as per USPI>Feb-2025
Rhinorrhoea >Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Vaginal discharge>Eligard>Unlisted as per CCDS>07-Nov-2024
Vaginal discharge>Eligard>Unlisted as per USPI>Feb-2025
Vaginal discharge>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Vaginal discharge>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

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Increased appetite>Eligard>Unlisted as per CCDS>07-Nov-2024
Increased appetite>Eligard>Unlisted as per USPI>Feb-2025
Increased appetite>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Increased appetite>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

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>02-Apr-2025

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>Unlisted as per USPI>Feb-2025
Off label use>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): The case is regarding 8 years old female child patient who experienced non serious events sneezing (sneezing), rhinorrhoea (transparent mucus), vaginal discharge (brown vaginal discharge), increased appetite (increased appetite), weight gain (weight gain) and off label use (patient was using Eligard 22.5 mg for central precocious puberty) during Eligard (leuprolide acetate) 22.5 milligram therapy for central precocious puberty. Tolmar assessed the reported events as non-serious since they did not meet the ICH seriousness criteria and are not IME events. The causality for the reported events sneezing, rhinorrhoea, vaginal discharge, increased appetite and weight gain is assessed as related with Eligard (drug) based on implied temporal relationship and known safety profile of Eligard and not related with device component of the drug. Causality for the event off label use is not related with Eligard (drug and device) components as the event happened due to human action, rather due to the product.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
WEIGHT	/May/2025		

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

1) Test Name: WEIGHT

Result Unstructured Data (free text) : Weight gain
Test Date: /May/2025

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]
Action(s) Taken With Drug : Dose not changed

Causality

1) Patient was using Eligard 22.5 mg for Central Precocious Puberty (Off label dosing - 10074165, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Sneezing (Sneezing - 10041232, Sneezing - 10041232)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Continuation Sheet for CIOMS report

3) Transparent mucus (Rhinorrhoea - 10039101, Rhinorrhoea - 10039101)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) Brown vaginal discharge (Vaginal discharge - 10046901, Vaginal discharge - 10046901)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
5) Increased appetite (Increased appetite - 10021654, Increased appetite - 10021654)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
6) Weight gain (Weight gain - 10047896, Weight increased - 10047899)
Causality as per reporter : Related
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) Sneezing
CORE UnLabeled
3) Transparent mucus
CORE Labeled
4) Brown vaginal discharge
CORE UnLabeled
5) Increased appetite
CORE UnLabeled
6) 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
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 dosing - 10074165, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Sneezing (Sneezing - 10041232, Sneezing - 10041232)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) Transparent mucus (Rhinorrhoea - 10039101, Rhinorrhoea - 10039101)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) Brown vaginal discharge (Vaginal discharge - 10046901, Vaginal discharge - 10046901)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
5) Increased appetite (Increased appetite - 10021654, Increased appetite - 10021654)
Causality as per reporter : Not Reported

Continuation Sheet for CIOMS report

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

6) 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 :

1) Patient was using Eligard 22.5 mg for Central Precocious Puberty
CORE
2) Sneezing
CORE
3) Transparent mucus
CORE
4) Brown vaginal discharge
CORE
5) Increased appetite
CORE
6) Weight gain
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 milligram, q 3 month