SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-05769

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
ESCM	NICARAGUA	12	Sep	2014	10	Female	27	Nov	2023

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

1) Weight gain of 4 kg (Weight gain (10047896), Weight increased (10047899))
(/Jun/2025 -) - Not Recovered/Not Resolved/Ongoing
2) Off-label use for non-approved indication (Off label use (10053762), Off label use (10053762))
(27/Nov/2023 -) - 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)

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) (27/Nov/2023 - 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
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-TLM-2025-05769
24c. DATE RECEIVED BY MANUFACTURER: 12/Aug/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 14/Aug/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-0066-20250812 (0)) on 12-Aug-2025 from a consumer (non-healthcare professional) regarding a child 10-year-old female patient who experienced non-serious events of ‘‘Off-label use for non-approved indication'' (off label use), and '' Weight gain of 4 kg'' (weight increased) during Eligard (Leuprolide acetate) 22.5 mg therapy for precocious puberty. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 13-Aug-2025.

The patient's medical history was unknown and current condition included precocious puberty.

Concomitant medication was unknown.

On 27-Nov-2023, the patient began receiving Eligard 22.5 mg, every 3 months, via subcutaneous route l precocious puberty (Lot numbers and Expiration dates were not provided).

On an unknown date in Jun-2025, the patient's weight increased by 4 kg. No further information was available.

Correction treatment was not reported.

Relevant test results included:
On an unknown date: Weight: Increased by 4 kg (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 off label use and weight increased was not recovered.

The reporter did not assess the seriousness of off label use and weight increased.

The reporter did not provide the causality of off label use in relationship to Eligard and Eligard unspecified device and assess the causality of weight increased in relationship to Eligard and Eligard unspecified device as related.

No further queries were raised.

Listedness:
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

Weight increased>Eligard>listed as per CCDS>07-Nov-2024
Weight increased>Eligard>unlisted as per USPI>Feb-2025
Weight increased>Eligard unspecified device>unlisted as per USPI>Feb-2025
Weight increased>Eligard>listed as per Canadian monograph>O2-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This case is regarding a child 10-year-old female patient for whom off label use (Off-label use for non-approved indication) was reported and experienced weight increased (Weight gain of 4 kg) during 22.5 mg Eligard therapy for precocious puberty. Tolmar assessed the events as non-serious since they did not meet the ICH seriousness criteria and are not IME events. The reported event off label use was considered as not related to Eligard as the event occurred with the product and not due to drug. Off label use is assessed as not related to device component of Eligard. 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...)

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

1) Test Name: WEIGHT
Result Unstructured Data (free text) : Increased by 4 kg
Test Date:

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

Product-Reaction Level

Continuation Sheet for CIOMS report

1) Drug : Eligard® (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
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 : 27/Nov/2023 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) Weight gain of 4 kg (Weight gain - 10047896, Weight increased - 10047899)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Off-label use for non-approved indication (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

Labeling :

1) Weight gain of 4 kg
CORE Labeled
2) Off-label use for non-approved indication
CORE UnLabeled

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) Weight gain of 4 kg (Weight gain - 10047896, Weight increased - 10047899)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Off-label use for non-approved indication (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

Labeling :

1) Weight gain of 4 kg
CORE
2) Off-label use for non-approved indication
CORE