CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-25NI058223

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year	Years		Day	Month	Year	
SBCR	NICARAGUA	14	Mar	2016	9	Female		Oct	2024	

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

1) from October 2024 to March 2025, she has gained 7 kilos/Weight gain (Abnormal weight gain (10000188), Abnormal weight gain (10000188))
(/Oct/2024 -) - Not Recovered/Not Resolved/Ongoing
2) Weight gain of 2 kg in 3 months (Weight gain (10047896), Weight increased (10047899))
(/Mar/2025 -) - Not Recovered/Not Resolved/Ongoing
3) High triglycerides (Triglycerides high (10052373), Blood triglycerides increased (10005839))
(06/Jun/2025 -) - Not Recovered/Not Resolved/Ongoing
4) Patient was using Eligard 22.5 mg for Central Precocious Puberty (Off label use in unapproved indication (10084345), Off label use (10053762))
Unknown

Cont..

- ☐ 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
(03-Oct-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

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-25NI058223
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
27/Jun/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
08/Jul/2025	☐ 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 Patient Support Program (reference number: NI-ADIUM-NI-0035-20250328) on 28-MAR-2025 from a Consumer/Other Non-Health Prof regarding a child 9-Year-old Female patient. It was reported that from OCT-2024 to MAR-2025, she had gained 7 kilograms (Abnormal weight gain), 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 01-APR-2025.

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

Concomitant medications were not reported.

On 03-OCT-2024, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for Central precocious puberty (Lot number and Expiration date were not reported).

On an unspecified date from OCT-2024 to MAR-2025, at an unknown time after the most recent dose of Eligard, the patient experienced had gained 7 kilograms.

Corrective treatment was not reported.

Relevant test results included:
On an unknown date in OCT-2024: Weight: 7 Kilogram (gained 7 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 Abnormal weight gain was Not Recovered.

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

On 27-Jun-2025, follow up information was received by Adium via Patient Support Program (reference number: NI-ADIUM-NI-0035-20250328) from a Consumer/Other Non-Health Prof regarding a Child 9-Year-old Female patient. New information added: Added new events: "High triglycerides" (Blood triglycerides increased), "Weight gain of 2 kg in 3 months" (weight increased) and "Patient was using Eligard 22.5 mg for Central Precocious Puberty" (off label use). Verbatim updated from "from October 2024 to March 2025, she has gained 7 kilos" to "from October 2024 to March 2025, she has gained 7 kilos/Weight gain". Lab test for triglycerides and weight gain was added. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 28-Jun-2025. Narrative updated.

Corrective treatment for weight gain was diet and for Blood triglycerides increased was Fenofibrate 100 mg daily for one month and Omega 31 gram daily for 3 months.

Relevant lab data:
On an unknown date: Triglycerides: High Triglycerides (Ref. range: Not provided).
On an unknown date: Weight gain: Weight gain of 2 kg in 3 months (Ref. range: Not provided).

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

The outcome of Blood triglycerides increased, and weight increased was not recovered.

The outcome of off label use was unknown.

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

The reporter did not assess the causality of off label use in relationship to Eligard and Eligard unspecified device.

The reporter assessed the causality of weight increased in relationship to Eligard and Eligard unspecified device as related.

The reporter assessed the causality of Blood triglycerides increased in relationship to Eligard and Eligard unspecified device as not related.

No further information is expected as the reporter did not consent to be contacted for follow-up.

Listedness:
Abnormal weight gain>Eligard>listed as per CCDS>07-Nov-2024
Abnormal weight gain>Eligard>Unlisted as per USPI>Feb-2025
Abnormal weight gain>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Abnormal weight gain>Eligard>listed as per Canadian monograph>O2-Apr-2025

weight increased>Eligard>listed as per CCDS>07-Nov-2024

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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

Blood triglycerides increased>Eligard>Unlisted as per CCDS>07-Nov-2024
Blood triglycerides increased>Eligard>Unlisted as per USPI>Feb-2025
Blood triglycerides increased>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Blood triglycerides increased>Eligard>Unlisted 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): This is regarding a child 9-Year-old Female patient who reported abnormal weight gain(from OCT-2024 to MAR-2025, she had gained 7 kilograms), weight increased (Weight gain of 2 kg in 3 months), Blood triglycerides increased (High triglycerides) 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. Abnormal weight gain, weight increased, Blood triglycerides increased were assessed as related to Eligard based on known product safety profile and not related to device component of Eligard.
Off label use is not related to Eligard (drug and device) as it is due to human action/error as per the reported information.

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
TRIGLYCERIDES	Unknown		
WEIGHT	Unknown	7 kilogram (kg)	
WEIGHT GAIN	Unknown		

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

3) Test Name: WEIGHT GAIN

Result Unstructured Data (free text) : Weight gain of 2 kg in 3 months

Test Date: Unknown

Lab Comments :

2) Test Name : WEIGHT

Lab Comments : gained 7 kilos

3) Test Name : WEIGHT GAIN

Lab Comments : Weight gain of 2 kg in 3 months

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

Continuation Sheet for CIOMS report

1) from October 2024 to March 2025, she has gained 7 kilos/Weight gain (Abnormal weight gain - 10000188, Abnormal weight gain - 10000188)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Weight gain of 2 kg in 3 months (Weight gain - 10047896, Weight increased - 10047899)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) High triglycerides (Triglycerides high - 10052373, Blood triglycerides increased - 10005839)
Causality as per reporter : Not Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) Patient was using Eligard 22.5 mg for Central Precocious Puberty (Off label use in unapproved indication - 10084345, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) from October 2024 to March 2025, she has gained 7 kilos/Weight gain
CORE Labeled
2) Weight gain of 2 kg in 3 months
CORE Labeled
3) High triglycerides
CORE UnLabeled
4) Patient was using Eligard 22.5 mg for Central Precocious Puberty
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) from October 2024 to March 2025, she has gained 7 kilos/Weight gain (Abnormal weight gain - 10000188, Abnormal weight gain - 10000188)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Weight gain of 2 kg in 3 months (Weight gain - 10047896, Weight increased - 10047899)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
3) High triglycerides (Triglycerides high - 10052373, Blood triglycerides increased - 10005839)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) Patient was using Eligard 22.5 mg for Central Precocious Puberty (Off label use in unapproved indication - 10084345, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) from October 2024 to March 2025, she has gained 7 kilos/Weight gain
CORE
2) Weight gain of 2 kg in 3 months
CORE
3) High triglycerides

Continuation Sheet for CIOMS report

CORE
4) Patient was using Eligard 22.5 mg for Central Precocious Puberty
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