SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-05533

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
PRIVACY	NICARAGUA	03	May	2015	10	Female	03	Feb	2025

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

1) Insulin resistance (Insulin resistance (10022489), Insulin resistance (10022489))
(/Jun/2025 -) - Not Recovered/Not Resolved/Ongoing
2) High cholesterol (High cholesterol (10020049), Blood cholesterol increased (10005425))
(/Jun/2025 -) - Not Recovered/Not Resolved/Ongoing
3) High triglycerides (Triglycerides high (10052373), Blood triglycerides increased (10005839))
(/Jun/2025 -) - Not Recovered/Not Resolved/Ongoing
4) Off-label use for non-approved indication (Off label use (10053762), Off label use (10053762))
(03/Feb/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) (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) (03/Feb/2025 - 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-2025-05533
24c. DATE RECEIVED BY MANUFACTURER: 05/Aug/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 13/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 Patient Support Program “ASOFARMA A TU LADO" (Reference number: NI-ADIUM-NI-0063-20250805 (0)) on 05-Aug-2025 from a consumer (non-healthcare professional) regarding a child, 10-year-old female patient who experienced non-serious events of ‘‘Insulin resistance" (Insulin resistance), "High cholesterol" (Blood cholesterol increased), "High triglycerides"(Blood triglycerides increased) and "Off-label use for non-approved indication"(Off label use) during Eligard (leuprolide acetate) 22.5 mg 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-Aug-2025.

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

Concomitant medications were not reported.

On 03-Feb-2025, the patient began receiving Eligard 22.5 mg once at every 3 month, via subcutaneous route, for central precocious puberty (Lot numbers and Expiration dates were not provided) off label use.

On an unknown date in Jun-2025, the patient experienced insulin resistance, high triglycerides and high cholesterol.

Corrective treatment for blood triglycerides increased and blood cholesterol increased included Omega 3: 2 capsules daily and for insulin resistance included Metformin 500 mg daily.

Relevant lab data included:
On an unknown date: Blood triglycerides: High (Ref range not provided).
On an unknown date: Blood cholesterol: High (Ref range not provided).

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

The outcome of insulin resistance, blood cholesterol increased, blood triglycerides increased and off label use was not recovered.

The reporter did not assess the seriousness of insulin resistance, blood cholesterol increased, blood triglycerides increased, and off label use.

The reporter assessed the causality of insulin resistance, blood cholesterol increased, blood triglycerides increased in relationship to Eligard and Eligard Unspecified device as not related.

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

No further queries were raised.

Listedness:
Insulin resistance>Eligard>Unlisted as per CCDS>07-Nov-2024
Insulin resistance>Eligard>Unlisted as per USPI>Feb-2025
Insulin resistance>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Insulin resistance>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Blood cholesterol increased>Eligard>Unlisted as per CCDS>07-Nov-2024
Blood cholesterol increased>Eligard>Unlisted as per USPI>Feb-2025
Blood cholesterol increased>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Blood cholesterol increased>Eligard>Unlisted as per Canadian monograph>02-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 10-year-old female patient who experienced insulin resistance (Insulin resistance), blood cholesterol increased(High cholesterol), blood triglycerides increased (High triglycerides) and had off label use (Off-label use for non-approved indication) during Eligard (leuprolide acetate) 22.5 mg 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. All the reported events were assessed as not related to Eligard (drug and device) considering the nature and etiology of reported events and inconsistency of the event with the product safety profile.

Continuation Sheet for CIOMS report

Additional Information (Continuation...)

Laboratory Data :

High

Lab Result :

Test Name	Test Date	Test Result	Normal Value
HIGH CHOLESTEROL	Unknown		
HIGH TRIGLYCERIDES	Unknown		

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

Product-Reaction Level

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 : 03/Feb/2025 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) Insulin resistance (Insulin resistance - 10022489, Insulin resistance - 10022489)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) High cholesterol (High cholesterol - 10020049, Blood cholesterol increased - 10005425)
Causality as per reporter : Not 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) 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) Insulin resistance
CORE UnLabeled
2) High cholesterol
CORE UnLabeled
3) High triglycerides
CORE UnLabeled
4) 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

Continuation Sheet for CIOMS report

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) Insulin resistance (Insulin resistance - 10022489, Insulin resistance - 10022489)

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

2) High cholesterol (High cholesterol - 10020049, Blood cholesterol increased - 10005425)

Causality as per reporter	:	Not 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) 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) Insulin resistance
   CORE
2) High cholesterol
   CORE
3) High triglycerides
   CORE
4) Off-label use for non-approved indication
   CORE