SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-06101

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
RCM	NICARAGUA	22	Oct	2015	9	Female	13	Feb	2025

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

1) 9-year-old female patient being treated with the medication Eligard 22.5 mg for 3 months for the indication of Central Precocious Puberty (Off label use in unapproved indication (10084345), Off label use (10053762))
(13/Feb/2025 -) - Unknown
2) Irritability (Irritability (10022998), Irritability (10022998))
(/May/2025 -) - Not Recovered/Not Resolved/Ongoing

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) (13/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-2025-06101
24c. DATE RECEIVED BY MANUFACTURER: 22/Aug/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 26/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 the Patient Support Program "ASOFARMA A TU LADO" (reference number: NI-ADIUM-NI-0072-20250822 (0)) on 22-Aug-2025 from a consumer (non-healthcare professional) regarding a child 9-year-old female patient who experienced non-serious events of ‘‘9-year-old female patient being treated with the medication Eligard 22.5 mg for 3 months for the indication of Central Precocious Puberty" (off label use) and "Irritability" (Irritability) 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 25-Aug-2025.

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

Concomitant medications were unknown.

On 13-Feb-2025, the patient started getting treated with Eligard 22.5 mg, every 3 months, via subcutaneous route for precocious puberty (Lot numbers and Expiration dates were not provided).

On an unknown date in May-2025, the patient experienced irritability. No further information was provided.

Correction treatment was unknown.

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

The outcome of irritability was not recovered and off label use was unknown.

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

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

No further queries were raised.

Listedness
off label use >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
off label use> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
off label use> Eligard®>unlisted as per USPI Eligard®>Feb-2025
off label use> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Irritability >Eligard® >listed as per CCDS Eligard®> 7-Nov-2024
Irritability > Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025
Irritability > Eligard®>unlisted as per USPI Eligard®>Feb-2025
Irritability > Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding a child 9-year-old female patient who experienced off label use (9-year-old female patient being treated with the medication Eligard 22.5 mg for 3 months for the indication of Central Precocious Puberty) and Irritability (Irritability) during Eligard (Leuprolide acetate) 22.5 mg therapy for precocious puberty. Tolmar assessed the reported events as non-serious since they did not meet the ICH seriousness criteria. The causality of event off label use was assessed as not related to suspect Eligard(drug and device) as the event occurred with the product due to human action rather than due to drug. The causality of event irritability was assessed as related to drug component of Eligard(not related to device) considering the known safety profile of the drug and close temporality. Age of the patient and precocious puberty could be confounders for the event.

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

Continuation Sheet for CIOMS report

Causality

1) 9-year-old female patient being treated with the medication Eligard 22.5 mg for 3 months for the indication of 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

2) Irritability (Irritability - 10022998, Irritability - 10022998)

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

Labeling :

1) 9-year-old female patient being treated with the medication Eligard 22.5 mg for 3 months for the indication of Central Precocious Puberty
CORE UnLabeled
2) Irritability
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) 9-year-old female patient being treated with the medication Eligard 22.5 mg for 3 months for the indication of Central Precocious Puberty (Off label use in unapproved indication - 10084345, Off label use - 10053762)

Causality as per reporter	: Not Reported
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2) Irritability (Irritability - 10022998, Irritability - 10022998)

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

Labeling :

1) 9-year-old female patient being treated with the medication Eligard 22.5 mg for 3 months for the indication of Central Precocious Puberty
CORE
2) Irritability
CORE