SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-03618

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	
GKAM	NICARAGUA	07	Dec	2017	7	Female	12	Mar	2025	

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

1) 7-year-old female patient being treated with the drug Eligard 22. 5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months (reported since March 12, 2025) for the indication Central Precocious Puberty (Off label use in unapproved indication (10084345), Off label use (10053762))
(12/Mar/2025 -) - Unknown
2) Irritability, more sensitive to the environment (Irritability (10022998), Irritability (10022998))
(26/Mar/2025 -) - Recovered/Resolved

- ☐ 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) (12/Mar/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-2025-03618
24c. DATE RECEIVED BY MANUFACTURER: 16/Jun/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 24/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...)

Event Description :

This study report from Nicaragua was received by Adium via Patient Support Program (reference number: NI-ADIUM-NI-0050-20250616 (0)) on 16-Jun-2025 from a consumer (non-health care professional) regarding a 07-year-old female child patient who experienced non-serious events of " 7-year-old female patient being treated with the drug Eligard 22. 5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months (reported since March 12, 2025) for the indication Central Precocious Puberty" (Off label use) and “Irritability, more sensitive to the environment” (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 17-Jun-2025.

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

Concomitant medications were unknown.

On 12-Mar-2025, the patient began receiving Eligard 22.5 mg, every 3 months, via subcutaneous route for precocious puberty (Lot numbers and Expiration dates were not provided) and had off-label use.

On 26-Mar-2025, the patient experienced mild irritability, more sensitive to the environment. No further details were available.

Corrective treatment was not reported.

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

The outcome of off label use was unknown.

The outcome of irritability was recovered.

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

The reporter did not provide the causality of off label use, while assessed the causality of irritability as related in relationship to Eligard and Eligard Unspecified device.

No further query was 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

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

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding a child 07-year-old female patient who had off label use (7-year-old female patient being treated with the drug Eligard 22. 5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months (reported since March 12, 2025) for the indication Central Precocious Puberty) and irritability (Irritability, more sensitive to the environment), during Eligard (leuprolide acetate) 22.5 mg therapy for precocious puberty. Tolmar assessed the events as non-serious since they do 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. The reported event irritability was considered as related as the contributory role of suspect drug Eligard cannot be ruled out considering known pharmacological profile of the drug. Event irritability was assessed as not related to the device component of Eligard.

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

Continuation Sheet for CIOMS report

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 : 12/Mar/2025 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) 7-year-old female patient being treated with the drug Eligard 22. 5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months (reported since March 12, 2025) for the indication 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, more sensitive to the environment (Irritability - 10022998, Irritability - 10022998)

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

Labeling :

1) 7-year-old female patient being treated with the drug Eligard 22. 5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months (reported since March 12, 2025) for the indication Central Precocious Puberty

CORE	UnLabeled

2) Irritability, more sensitive to the environment

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) 7-year-old female patient being treated with the drug Eligard 22. 5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months (reported since March 12, 2025) for the indication 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, more sensitive to the environment (Irritability - 10022998, Irritability - 10022998)

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

Labeling :

1) 7-year-old female patient being treated with the drug Eligard 22. 5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months (reported since March 12, 2025) for the indication Central Precocious Puberty

CORE

2) Irritability, more sensitive to the environment

CORE