SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-02952

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE Years	3. SEX	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year			Day	Month	Year	
ASCJ	NICARAGUA	09	Aug	2016	8	Female	10	Mar	2025	

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

1) Sudden mood changes (Mood altered (10027940), Mood altered (10027940))
(24/Mar/2025 -) - Not Recovered/Not Resolved/Ongoing
2) patient under treatment with the drug Eligard 22.5 mg every 3 months for central precocious puberty (Off label dosing (10074165), Off label use (10053762))
(10/Mar/2025 -) - Unknown

- ☐ 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) (10/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
debbie.maierhofer@tolmar.comand+1-4129158447

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-2025-02952
24c. DATE RECEIVED BY MANUFACTURER: 02/Jun/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 11/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 Brazil was received by Adium (reference number: NI-ADIUM-NI-0049-20250602) on 02-Jun-2025, by the reporter, Patient or family member or other non-health professional regarding a child of 8-year-old female patient who experienced a non-serious event of “Sudden mood changes” (Mood altered) and “Off-label doing” (Off label use) during Eligard (leuprolide acetate) 22.5 mg therapy for an Central Precocious Puberty indication. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 03-Jun-2025.

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

Concomitant medications were unknown.

On 10-Mar-2025, the patient began receiving Eligard 22.5 mg, every 3 month via Subcutaneous route for Central Precocious Puberty indication (Lot numbers and Expiration date was not reported).

On 24-Mar-2025, patient experienced sudden mood swings. No further details were available.

Corrective treatment was not reported.

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

The outcome of Off-label use was unknown.

The outcome of Mood altered was Not recovered / not resolved.

The reporter did not assess the seriousness of Off-label use and Mood altered.

The reporter assessed the causality of Mood altered in relationship to Eligard and Eligard Unspecified device as related.

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

The reporter consent to be contacted for follow-up.

Listedness

Mood altered>Eligard>Unlisted as per CCDS>07-Nov-2024
Mood altered>Eligard>Unlisted as per USPI>Feb-2025
Mood altered>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Mood altered>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 08-year-old female patient who had who had Mood altered (Sudden mood changes) and Off label use (patient under treatment with the drug Eligard 22.5 mg every 3 months for central precocious puberty) during Eligard (leuprolide acetate) 22.5 mg therapy for prostate cancer. Tolmar assessed other events as non-serious since they do not meet the ICH seriousness criteria and are not an IME event. The reported event mood altered was assessed as related to Eligard (drug) in view of time to onset of event and pharmacological profile of drug and assessed as not related to device component of Eligard. The reported event off label use was assessed as not related to Eligard (drug and device) as the event occurred with the product due to human/prescriber action, rather due to the drug.

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

Continuation Sheet for CIOMS report

Indications	:	1) Central Precocious Puberty [10073186 - Central precocious puberty]
Therapy Dates	:	1) From : 10/Mar/2025 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) Sudden mood changes (Mood altered - 10027940, Mood altered - 10027940)

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

2) patient under treatment with the drug Eligard 22.5 mg every 3 months for central precocious puberty (Off label dosing - 10074165, Off label use - 10053762)

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

Labeling :

1) Sudden mood changes

CORE	UnLabeled

2) patient under treatment with the drug Eligard 22.5 mg every 3 months 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
Route of Admin	:	1) Subcutaneous
Indications	:	1) Central Precocious Puberty [10073186 - Central precocious puberty]
Action(s) Taken With Drug	:	Not applicable

Causality

1) Sudden mood changes (Mood altered - 10027940, Mood altered - 10027940)

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

2) patient under treatment with the drug Eligard 22.5 mg every 3 months for central precocious puberty (Off label dosing - 10074165, Off label use - 10053762)

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

Labeling :

1) Sudden mood changes
CORE

2) patient under treatment with the drug Eligard 22.5 mg every 3 months for central precocious puberty
CORE