SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-06139

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	
PRIVACY	NICARAGUA	07	May	2018	7	Female	18	Jun	2025	

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

1) Isolation, does not want to leave the room (Social problem (10062254), Social problem (10062254))
(/Jul/2025 -) - Not Recovered/Not Resolved/Ongoing
2) Off-label use for non-approved indication (Off label use (10053762), Off label use (10053762))
(18/Jun/2025 -) - Unknown
3) Cries (Crying (10011469), Crying (10011469))
(/Jul/2025 -) - Not Recovered/Not Resolved/Ongoing

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) (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) (18/Jun/2025 -)	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

1)MELATONIN(MELATONIN)

Cont..

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-2025-06139
24c. DATE RECEIVED BY MANUFACTURER: 25/Aug/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 27/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...)

4) Insomnia (Insomnia (10022437), Insomnia (10022437)(/Aug/2025 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This study report from Nicaragua was received by Adium via Patient Support Programme (Reference number: NI-ADIUM-NI-0074-20250825) on 25-Aug-2025 from a consumer (non-healthcare professional) regarding a child, 7-year-old female patient who experienced non-serious events of ‘‘Cries'' (Crying), "Isolation, does not want to leave the room" (Social problem), "Insomnia" (Insomnia) 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 26-Aug-2025.

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

Concomitant medications were Melatonin.

On an unknown date, the patient began receiving Eligard 22.5 mg at a frequency of one in every three months, via subcutaneous route, for Central precocious puberty (Lot numbers and Expiration dates were not provided).

On 18-Jun-2025, the patient received the last dose of Eligard 22.5 mg, via subcutaneous route, for Central precocious puberty (Lot numbers and Expiration dates were not provided).

On an unknown date in Jul-2025, the patient has experienced that she was crying for no reason, was leaving in isolation and did not want to leave the room.

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

Corrective treatment was not reported.

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

The outcome of crying, social problem and Insomnia was not recovered and that of Off-label use was unknown.

The reporter did not assess the seriousness of crying, social problem, Insomnia and Off-label use.

The reporter assessed the causality of Crying and Social problem in relationship to Eligard and Eligard unspecified device as related.

The reporter assessed the causality of insomnia 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 information is expected as consent to be contacted was not provided.

Listedness:

Crying>Eligard>listed as per CCDS>07-Nov-2024
Crying>Eligard>listed as per USPI>Feb-2025
Crying>Eligard Unspecified Device>listed as per USPI>Feb-2025
Crying>Eligard>listed as per Canadian monograph>02-Apr-2025

Insomnia >Eligard>listed as per CCDS>07-Nov-2024
Insomnia >Eligard>listed as per USPI>Feb-2025
Insomnia >Eligard Unspecified Device>listed as per USPI>Feb-2025
Insomnia >Eligard>listed as per Canadian monograph>02-Apr-2025

Social problem>Eligard>Unlisted as per CCDS>07-Nov-2024
Social problem>Eligard>Unlisted as per USPI>Feb-2025
Social problem>Eligard Unspecified Device>Unlisted as per USPI>Feb-2025
Social problem>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) :

Continuation Sheet for CIOMS report

Evaluators comments : As per company conventions, the events crying, social problem, Insomnia and Off-label use are considered with not applicable causality by default. The events are unlisted/unexpected with reference to the current CCDS/SmPC and as per company conventions. All the events are non-serious. The benefit-risk profile of Eligard (Drug and device) is not adversely affected by this report.

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 : 18/Jun/2025 To :Unknown
Action(s) Taken With Drug : Unknown

Causality

1) Isolation, does not want to leave the room (Social problem - 10062254, Social problem - 10062254)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) 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
3) Cries (Crying - 10011469, Crying - 10011469)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
4) Insomnia (Insomnia - 10022437, Insomnia - 10022437)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Isolation, does not want to leave the room
CORE UnLabeled
2) Off-label use for non-approved indication
CORE UnLabeled
3) Cries
CORE Labeled
4) Insomnia
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) Isolation, does not want to leave the room (Social problem - 10062254, Social problem - 10062254)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Off-label use for non-approved indication (Off label use - 10053762, Off label use - 10053762)

Continuation Sheet for CIOMS report

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

3) Cries (Crying - 10011469, Crying - 10011469)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Insomnia (Insomnia - 10022437, Insomnia - 10022437)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Isolation, does not want to leave the room
CORE
2) Off-label use for non-approved indication
CORE
3) Cries
CORE
4) Insomnia
CORE

22.CONCOMITANT DRUG(S) (Continuation...)

1). Drug : MELATONIN
Active Substance : 1) MELATONIN
Form Strength :
Indications : 1) Drug use for unknown indication [10057097 - Drug use for unknown indication]