SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-01045

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
LMML	NICARAGUA	20	Jun	2016	8	Female	24	Apr	2024

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

1) Skin itching (Itchy (10023089), Pruritus (10037087))
(/May/2024 -) - Not Recovered/Not Resolved/Ongoing
2) Anxiety (Anxiety (10002855), Anxiety (10002855))
(/Dec/2024 -) - Not Recovered/Not Resolved/Ongoing
3) Big appetite (Increased appetite (10021654), Increased appetite (10021654))
(/Dec/2024 -) - Not Recovered/Not Resolved/Ongoing
4) Hyperactivity (Psychomotor hyperactivity (10037211), Psychomotor hyperactivity (10037211))
(/Dec/2024 -) - 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) (22.5 Milligram, 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 [10058084 - Precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (24/Apr/2024 - 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-2025-01045
24c. DATE RECEIVED BY MANUFACTURER: 24/Apr/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 05/May/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...)

5) Patient is receiving 22.5 mg for central precocious puberty (Drug use for unapproved dosing regimen (10076468), Product use issue (10076309)(24/Apr/2024 -) - Not Recovered/Not Resolved/Ongoing)

6) White spot with relief approximately 5 cm long and slightly itchy (Rash macular (10037867), Rash macular (10037867)(/May/2024 -) - Not Recovered/Not Resolved/Ongoing)

7) Allergic reaction to Eligard (Hypersensitivity (10020751), Hypersensitivity (10020751)(/May/2024 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This study report from Brazil was received via Adium (reference number: NI-ADIUM-NI-0041-2025042) on 24-Apr-2025 from a consumer (patient's mother) (non-healthcare professional) regarding a child 08-year-old female patient who experienced non-serious events of "White spot with relief approximately 5 cm long and slightly itchy" (Rash macular), “Skin itching” (Pruritus), “Allergic reaction to Eligard” (Hypersensitivity), “Anxiety” (Anxiety), “Hyperactivity” (Psychomotor hyperactivity) and “Big appetite” (Increased appetite) during Eligard (leuprolide acetate) 22.5 mg therapy for central precocious puberty (Product use issue). The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 25-Apr-2025.

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

Concomitant medications were unknown.

On 24-Apr-2024, the patient began receiving Eligard 22.5 mg, every 3 months, via subcutaneous route for central precocious puberty (Lot number and Expiration dates were not reported).

On an unspecified date of May-2024, the patient experienced a white spot with relief appeared on her right thigh, approximately 5 cm long, which was slightly itchy. No further details were available.

On an unspecified date of Oct-2024, she noticed that the spot had increased in size, but it was no longer itchy. She went to the dermatologist and he said that it was a mole, but she was not convinced of the diagnosis, so she went to another dermatologist and the dermatologist said that it was an allergic reaction to Eligard since it had appeared in the days following its application, but that with time it was possible that the lesion would disappear. No further details were available.

On an unspecified date of Dec-2024, it was also reported that she had been suffering from anxiety, hyperactivity, and great appetite. No further details were available.

Corrective 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 rash macular, pruritus, hypersensitivity, anxiety, psychomotor hyperactivity, increased appetite and Product use issue was not recovered.

The reporter did not assess the seriousness of rash macular, pruritus, hypersensitivity, anxiety, psychomotor hyperactivity, increased appetite and Product use issue.

The reporter did not provide the causality of rash macular, pruritus, hypersensitivity, anxiety, psychomotor hyperactivity, increased appetite and Product use issue in relationship to Eligard and Eligard Unspecified device.

Listedness

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

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

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

Continuation Sheet for CIOMS report

Product use issue>Eligard>Unlisted as per CCDS>07-Nov-2024
Product use issue>Eligard>Unlisted as per USPI>Feb-2025
Product use issue>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Product use issue>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

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

Rash macular>Eligard>Listed as per CCDS>07-Nov-2024
Rash macular>Eligard>Listed as per USPI>Feb-2025
Rash macular>Eligard unspecified device>Listed as per USPI>Feb-2025
Rash macular>Eligard>Listed as per Canadian monograph>02-Apr-2025

Hypersensitivity>Eligard>Listed as per CCDS>07-Nov-2024
Hypersensitivity>Eligard>Listed as per USPI>Feb-2025
Hypersensitivity>Eligard unspecified device>Listed as per USPI>Feb-2025
Hypersensitivity>Eligard>Listed 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, rash macular ("White spot with relief approximately 5 cm long and slightly itchy"), pruritus (“Skin itching”), hypersensitivity (“Allergic reaction to Eligard”), anxiety(anxiety), psychomotor hyperactivity (Hyperactivity) and increased appetite (“Big appetite”) during Eligard (leuprolide acetate) 22.5 mg therapy for central precocious puberty (Product use issue). Tolmar assessed the event as non-serious since it does not meet the ICH seriousness criteria and is not an IME event. The causality of the reported event product use issue was assessed as not related to Eligard (drug and device) as the event occurred with the product due to human action, rather due to the drug. Tolmar assessed all other reported events as related to Eligard (drug) based on the known safety profile of the drug and not related to device.

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

Product-Reaction Level

1) Drug	:	Eligard® (Leuprolide acetate)
Active Substance	:	1) Leuprolide acetate
Drug Characterization	:	Suspect
Form Strength	:	1) 22.5 Milligram
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 [10058084 - Precocious puberty]
Therapy Dates	:	1) From : 24/Apr/2024 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) Skin itching (Itchy - 10023089, Pruritus - 10037087)		
Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable
2) Anxiety (Anxiety - 10002855, Anxiety - 10002855)		
Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable
3) Big appetite (Increased appetite - 10021654, Increased appetite - 10021654)		
Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable
4) Hyperactivity (Psychomotor hyperactivity - 10037211, Psychomotor hyperactivity - 10037211)		
Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Related
DeChallenge	:	Not applicable

Continuation Sheet for CIOMS report

ReChallenge : Not Applicable

5) Patient is receiving 22.5 mg for central precocious puberty (Drug use for unapproved dosing regimen - 10076468, Product use issue - 10076309)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) White spot with relief approximately 5 cm long and slightly itchy (Rash macular - 10037867, Rash macular - 10037867)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) Allergic reaction to Eligard (Hypersensitivity - 10020751, Hypersensitivity - 10020751)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Skin itching
CORE UnLabeled
2) Anxiety
CORE UnLabeled
3) Big appetite
CORE UnLabeled
4) Hyperactivity
CORE UnLabeled
5) Patient is receiving 22.5 mg for central precocious puberty
CORE UnLabeled
6) White spot with relief approximately 5 cm long and slightly itchy
CORE Labeled
7) Allergic reaction to Eligard
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 [10058084 - Precocious puberty]
Action(s) Taken With Drug : Not applicable

Causality

1) Skin itching (Itchy - 10023089, Pruritus - 10037087)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Anxiety (Anxiety - 10002855, Anxiety - 10002855)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Big appetite (Increased appetite - 10021654, Increased appetite - 10021654)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Hyperactivity (Psychomotor hyperactivity - 10037211, Psychomotor hyperactivity - 10037211)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) Patient is receiving 22.5 mg for central precocious puberty (Drug use for unapproved dosing regimen - 10076468, Product use issue - 10076309)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Continuation Sheet for CIOMS report

6) White spot with relief approximately 5 cm long and slightly itchy (Rash macular - 10037867, Rash macular - 10037867)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) Allergic reaction to Eligard (Hypersensitivity - 10020751, Hypersensitivity - 10020751)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Skin itching
CORE
2) Anxiety
CORE
3) Big appetite
CORE
4) Hyperactivity
CORE
5) Patient is receiving 22.5 mg for central precocious puberty
CORE
6) White spot with relief approximately 5 cm long and slightly itchy
CORE
7) Allergic reaction to Eligard
CORE