SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-04333

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	
MMU	NICARAGUA	27	Nov	2020	4	Female	02	Apr	2025	

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

1) Brown vaginal discharge (Vaginal discharge (10046901), Vaginal discharge (10046901))
(05/Apr/2025 - 06/Apr/2025) - Recovered/Resolved
2) 22.5 mg every 3 months for the indication Central Precocious Puberty (Off label use in unapproved indication (10084345), Off label use (10053762))
(02/Apr/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) (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 [10073186 - Central precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (02/Apr/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) PRECOCIOUS PUBERTY (10058084, 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-2025-04333
24c. DATE RECEIVED BY MANUFACTURER: 02/Jul/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 08/Jul/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 Programme (Reference number: NI-ADIUM-NI-0052-20250702) on 02-Jul-2025 from a reporter (consumer or non-healthcare professional) regarding a child, 04-year-old female patient who experienced non-serious event of ''brown vaginal discharge" (vaginal discharge) and "22.5 mg every 3 months for the indication central precocious puberty" (off label use) 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 03-Jul-2025.

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

Concomitant medication was unknown.

On 02-Apr-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).

On 05-Apr-2025, the patient mother stated that patient began to experience brown vaginal discharge that lasted for two days. No further details were provided.

Corrective treatment was unknown.

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

On 06-Apr-2025, the outcome of vaginal discharge was resolved.

The outcome of off label use was unknown.

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

The reporter provided the causality of vaginal discharge 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.

No further query was raised.

Listedness:
Vaginal discharge>Eligard>Unlisted as per CCDS>07-Nov-2024
Vaginal discharge>Eligard>Unlisted as per USPI>Feb-2025
Vaginal discharge>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Vaginal discharge>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, 04-year-old female patient who experienced vaginal discharge (brown vaginal discharge) and off label use (22.5 mg every 3 months for the indication central precocious puberty) 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. Vaginal discharge was assessed as related to Eligard drug based on temporal association and increase in clinical signs and symptoms of puberty may be observed during the first weeks of therapy. Vaginal discharge was assessed as not related to device component of Eligard. The causality of the 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 the drug.

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

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 : 02/Apr/2025 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) Brown vaginal discharge (Vaginal discharge - 10046901, Vaginal discharge - 10046901)

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

2) 22.5 mg every 3 months 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

Labeling :

1) Brown vaginal discharge

CORE	UnLabeled

2) 22.5 mg every 3 months for the indication 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
Indications	:	1) Central Precocious Puberty [10073186 - Central precocious puberty]
Action(s) Taken With Drug	:	Not applicable

Causality

1) Brown vaginal discharge (Vaginal discharge - 10046901, Vaginal discharge - 10046901)

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

2) 22.5 mg every 3 months 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

Labeling :

1) Brown vaginal discharge
CORE

2) 22.5 mg every 3 months for the indication Central Precocious Puberty
CORE