SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-00967

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	
GEPC	NICARAGUA	21	Apr	2015	10	Female	24	Jan	2025	

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

1) Heavy vaginal bleeding (Bleeding vaginal (10005143), Vaginal haemorrhage (10046910))
(06/Feb/2025 -) - Recovered/Resolved
2) Eligard 22.5 mg every 3 months for Central Precocious Puberty (Drug use for unapproved dosing regimen (10076468), Product use issue (10076309))
(24/Jan/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)	16. ROUTE(S) OF ADMINISTRATION
1) (22.5 milligram(s), 1 in 3 Month)	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) (24/Jan/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-2025-00967
24c. DATE RECEIVED BY MANUFACTURER: 23/Apr/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 03/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...)

Event Description :

This study report from Nicaragua was received by Adium via the 'ASOFARMA A TU LADO' Patient Support Program (reference number: NI-ADIUM-NI-0040-20250423) on 23-Apr-2025 from a consumer (patient's mother) (non-healthcare professional) regarding a child of 10-year-old female patient who experienced non-serious events of 'heavy vaginal bleeding" (Vaginal haemorrhage) and 'Eligard 22.5 mg every 3 months for Precocious Puberty ' (Product use issue) during Eligard (Leuprolide acetate) 22.5 milligram 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 25-Apr-2025.

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

Concomitant medications were unknown.

On 24-Jan-2025, the patient began receiving Eligard 22.5 mg, every 3 months via subcutaneous route for central precocious puberty (Lot numbers and Expiration dates were not provided).

On 06-Feb-2025, the patient started bleeding from the vagina in abundant quantity, which lasted between 5 and 6 days. 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 vaginal haemorrhage was resolved, and that of product use issue was unknown.

The reporter did not assess the seriousness of vaginal haemorrhage and product use issue.

The reporter did not provide the causality of vaginal haemorrhage and product use issue in relationship to Eligard and Eligard unspecified device.

No further queries were raised.

Listedness

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 needle>Unlisted as per USPI>Feb-2025
Product use issue>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Vaginal haemorrhage>Eligard>Listed as per CCDS>07-Nov-2024
Vaginal haemorrhage>Eligard>Unlisted as per USPI>Feb-2025
Vaginal haemorrhage>Eligard Unspecified needle>Unlisted as per USPI>Feb-2025
Vaginal haemorrhage>Eligard>Listed as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding a child 10-year-old female patient who had Vaginal haemorrhage ('heavy vaginal bleeding") and Product use issue ('Eligard 22.5 mg every 3 months for Central Precocious Puberty) during Eligard (Leuprolide acetate) 22.5 milligram therapy for central precocious puberty. Tolmar assessed the event as non-serious since it does not meet the ICH seriousness criteria and is not an IME event. 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. The reported event vaginal haemorrhage is assessed as related to Eligard (drug) based on the known safety profile of the drug and not related to 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
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 : 24/Jan/2025 To :Continuing

Continuation Sheet for CIOMS report

Action(s) Taken With Drug : Dose not changed

Causality

1) Heavy vaginal bleeding (Bleeding vaginal - 10005143, Vaginal haemorrhage - 10046910)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Eligard 22.5 mg every 3 months 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

Labeling :

1) Heavy vaginal bleeding
CORE Labeled
2) 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
Indications : 1) Precocious puberty [10058084 - Precocious puberty]
Action(s) Taken With Drug : Not applicable

Causality

1) Heavy vaginal bleeding (Bleeding vaginal - 10005143, Vaginal haemorrhage - 10046910)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Eligard 22.5 mg every 3 months 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

Labeling :

1) Heavy vaginal bleeding
CORE
2) Eligard 22.5 mg every 3 months for Central Precocious Puberty
CORE