SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-00688

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
VGBB	NICARAGUA	04	Nov	2016	8	Female	02	Apr	2025

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

1) Eligard 22.5 mg every 3 months was used for central precocious puberty (Off label dosing (10074165), Off label use (10053762))
(02/Apr/2025 -) - Unknown
2) Belly pain (Abdominal pain (10000081), Abdominal pain (10000081))
(15/Apr/2025 -) - Not Recovered/Not Resolved/Ongoing
3) Heavy vaginal bleeding (Vaginal haemorrhage (10046910), Vaginal haemorrhage (10046910))
(15/Apr/2025 -) - Not Recovered/Not Resolved/Ongoing

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..

15. DAILY DOSE(S)

1) (22.5, 1 in 3 Month)

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous

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)	

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☑ NA

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ NA

(NA : Not Applicable)

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-2025-00688
24c. DATE RECEIVED BY MANUFACTURER: 15/Apr/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 26/Apr/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 (reference number: NI-ADIUM-NI-0038-20250415) via an e-mail from Patient Support Program on 15-Apr-2025, from a consumer (patient's mother/ family member) regarding a 08-year-old female child patient who experienced non-serious events of ‘heavy vaginal bleeding' (vaginal haemorrhage), ‘belly pain' (abdominal pain) and 'Eligard 22.5 mg every 3 months was used for 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 16-Apr-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 as off label use (Lot numbers and Expiration dates were not reported). No further details were provided.

On 15-Apr-2025, the patient's mother reported that the patient had abundant vaginal bleeding in the morning that was associated with belly pain/pain in the abdomen. No further details were provided.

Corrective treatment was unknown.

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

The outcome of vaginal haemorrhage, abdominal pain was not resolved, and off label use was unknown.

The reporter did not assess the seriousness of vaginal haemorrhage, off label use and abdominal pain.

The reporter did not provide the causality of vaginal haemorrhage, off label use and abdominal pain in relationship to Eligard and Eligard Unspecified Device.

No follow up queries were raised.

Listedness
Off label use >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
Off label use> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
Off label use> Eligard®>unlisted as per USPI Eligard®>Feb-2025
Off label use> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Abdominal pain >Eligard® >listed as per CCDS Eligard®> 7-Nov-2024
Abdominal pain> Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025
Abdominal pain> Eligard®>unlisted as per USPI Eligard®>Feb-2025
Abdominal pain> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Vaginal haemorrhage >Eligard® >listed as per CCDS Eligard®> 7-Nov-2024
Vaginal haemorrhage> Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025
Vaginal haemorrhage> Eligard®>unlisted as per USPI Eligard®>Feb-2025
Vaginal haemorrhage> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Company comment (Tolmar): This is regarding a child, 8-year-old female patient who reported vaginal haemorrhage (heavy vaginal bleeding), abdominal pain (belly pain) and off label use (Eligard 22.5 mg every 3 months was used for 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. The causality of 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. The causality of events vaginal haemorrhage and abdominal pain was assessed as related to suspect drug Eligard(not related to device) considering the close temporality, known safety profile of the drug and age of the patient could be a risk factor.

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

Continuation Sheet for CIOMS report

Form of Admin	:	1) Injection
Lot Number	:	1) Unknown
Daily Dose	:	(22.5, 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) Eligard 22.5 mg every 3 months was used 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

2) Belly pain (Abdominal pain - 10000081, Abdominal pain - 10000081)

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

3) Heavy vaginal bleeding (Vaginal haemorrhage - 10046910, Vaginal haemorrhage - 10046910)

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

Labeling :

1) Eligard 22.5 mg every 3 months was used for central precocious puberty
   CORE UnLabeled
2) Belly pain
   CORE Labeled
3) Heavy vaginal bleeding
   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) Eligard 22.5 mg every 3 months was used 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

2) Belly pain (Abdominal pain - 10000081, Abdominal pain - 10000081)

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

3) Heavy vaginal bleeding (Vaginal haemorrhage - 10046910, Vaginal haemorrhage - 10046910)

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

Labeling :

1) Eligard 22.5 mg every 3 months was used for central precocious puberty
   CORE
2) Belly pain
   CORE
3) Heavy vaginal bleeding
   CORE

15. DAILY DOSE(S) (Continuation...)

Continuation Sheet for CIOMS report

Dosage Text :
Drug 1 :Eligard®
1) ELIGARD 22.5 MG x 1 LIO x 2 JER