

SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-00688

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last) VGBB	1a. COUNTRY NICARAGUA	2. DATE OF BIRTH Day 04 Month Nov Year 2016	2a. AGE Years 8	3. SEX Female	4-6 REACTION ONSET Day 15 Month Apr Year 2025	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
7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) 1) Female patient was treated with Eligard 22.5 mg every 3 months for central precocious puberty (Off label dosing (10074165), Off label use (10053762)) (15/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 4) Daily headache (Headache (10019211), Headache (10019211)) (/May/2025 -) - Not Recovered/Not Resolved/Ongoing						

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S)(include generic name) 1) Eligard® (Leuprolide acetate, Leuprolide acetate) (Suspect) (22.5 Milligram, Injection)(Unknown)		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) 1) (02/Apr/2025 - Ongoing)	19. THERAPY DURATION	

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 Anjan.Chatterjee@tolmar.comand+1--9702124900		Study Information Study Name: NA EudraCT Number: Protocol No.: NA Center No.: Subject Id :	
24. REPORT NULLIFIED ☐ YES ☐ NO	24b. MFR CONTROL NO. NI-Tolmar-TLM-2025-00688		
24c. DATE RECEIVED BY MANUFACTURER 01/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 (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 'Female patient was treated with Eligard 22.5 mg every 3 months 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.

On 01-Jul-2025, follow-up information was received by Adium via Patient Support Programme (reference number: NI-ADIUM-NI-0038-20250415 (1)) from a consumer (non-healthcare professional) and sent to Tolmar on 03-Jul-2025. New information included: Added a new non-serious event of "Daily headache" (Headache) and a treatment medication.

On an unknown date in May-2025, the patient began experiencing a daily headache, described as mild in intensity.

Corrective treatment included ibuprofen.

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

The outcome of headache was not recovered.

The reporter did not assess the seriousness of headache.

The reporter did not provide the causality of headache 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

Continuation Sheet for CIOMS report

Headache >Eligard® >listed as per CCDS Eligard®> 7-Nov-2024
 Headache > Eligard® >listed as per Canadian Monograph Eligard®> 2-Apr-2025
 Headache > Eligard®>unlisted as per USPI Eligard®>Feb-2025
 Headache > 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 (Female patient was treated with Eligard 22.5 mg every 3 months 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.

Follow up added event of headache(headache). Tolmar assessed the reported event as non-serious since it did not meet the ICH seriousness criteria. The causality of event headache was assessed as related to suspect Eligard(drug) and not related to device considering the known safety profile of 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
 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) Female patient was treated with Eligard 22.5 mg every 3 months 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

4) Daily headache (Headache - 10019211, Headache - 10019211)

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

Labeling :

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

Continuation Sheet for CIOMS report

4) Daily headache
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) Female patient was treated with Eligard 22.5 mg every 3 months 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

4) Daily headache (Headache - 10019211, Headache - 10019211)

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

Labeling :

1) Female patient was treated with Eligard 22.5 mg every 3 months for central precocious puberty

CORE

2) Belly pain

CORE

3) Heavy vaginal bleeding

CORE

4) Daily headache

CORE

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

Dosage Text :

Drug 1 :Eligard®

1) ELIGARD 22.5 MG x 1 LIO x 2 JER