CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

NI-Tolmar-TLM-2025-05242

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
LMAP	NICARAGUA	11	May	2017	8	Female	29	Jan	2025

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

1) Vaginal discharge of mucus (Vaginal discharge (10046901), Vaginal discharge (10046901))
(25/Jul/2025 - 25/Jul/2025) - Recovered/Resolved
2) Eligard 22.5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months for the indication of Central Precocious Puberty (Off label dosing (10074165), Off label use (10053762))
(29/Jan/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) (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) (29/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
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-2025-05242
24c. DATE RECEIVED BY MANUFACTURER: 29/Jul/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 05/Aug/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-0062-20250729 (0)) on 29-Jul-2025 from a consumer (patient's family member) (non-healthcare professional) regarding a child, 8-year-old female patient who experienced non-serious events of 'Vaginal discharge of mucus' (Vaginal discharge), and 'Eligard 22.5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months for the indication of 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 30-Jul-2025.

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

Concomitant medications were unknown.

On 29-Jan-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 25-Jul-2025, the patient experienced vaginal mucus discharge. No further details were provided.

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.

On 25-Jul-2025, the outcome of vaginal discharge was recovered.

The outcome of off label use was not recovered.

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

The reporter did not provide the causality of off label use while assessed the causality of vaginal discharge as related in relationship to Eligard and Eligard unspecified device.

No further queries were 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 case is regarding a 08-year-old female patient for whom off label use (Eligard 22.5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months for the indication of Central Precocious Puberty) and vaginal discharge (Vaginal discharge of mucus) was reported during 22.5 mg Eligard therapy for 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 off label use was considered as not related to Eligard as the event occurred with the product and not due to drug. Off label use is assessed as not related to device component of Eligard. Event vaginal discharge was assessed as not related to Eligard (Drug and device) due to inconsistency with the product safety profile and pubertal age group of the patient could be the confounding factor.

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)

Continuation Sheet for CIOMS report

Route of Admin : 1) Subcutaneous
Indications : 1) Central Precocious Puberty [10073186 - Central precocious puberty]
Therapy Dates : 1) From : 29/Jan/2025 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) Vaginal discharge of mucus (Vaginal discharge - 10046901, Vaginal discharge - 10046901)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Eligard 22.5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months for the indication of 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

Labeling :

1) Vaginal discharge of mucus
CORE UnLabeled
2) Eligard 22.5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months for the indication of 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) Vaginal discharge of mucus (Vaginal discharge - 10046901, Vaginal discharge - 10046901)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Eligard 22.5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months for the indication of 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

Labeling :

1) Vaginal discharge of mucus
CORE
2) Eligard 22.5 mg lyophilized for injectable suspension at a dose of 22.5 mg every 3 months for the indication of Central Precocious Puberty
CORE