SUSPECT ADVERSE REACTION REPORT

NI-TOLMAR, INC.-25NI057156

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	4-6 REACTION ONSET		
		Day	Month	Year	Years		Day	Month	Year
EACM	NICARAGUA	25	Feb	2017	7	Female	22	Nov	2024

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

1) OCCASIONAL KNEE PAIN WHEN WALKING (Knee pain (10023477), Arthralgia (10003239))
(25/Jan/2025 -) - Not Recovered/Not Resolved/Ongoing
2) Nose and chin pimples (Pimples (10035049), Acne (10000496))
(/May/2025 -) - Not Recovered/Not Resolved/Ongoing
3) Pellets on hands and feet (Skin disorder (10040831), Skin disorder (10040831))
(/May/2025 -) - Recovering/Resolving
4) Eligard 22.5 mg every 3 months (Off label dosing (10074165), Off label use (10053762))
(22/Nov/2024 -) - Unknown

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)(Asked but 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) (22/Nov/2024 - 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, INC.-25NI057156
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
23/May/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
03/Jun/2025	☑ 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 Asofarma a tu lado Patient Support Program (reference number: NI-ADIUM-NI-0022-20250225) on 25-FEB-2025 from a Consumer/Other Non-Health Prof regarding a Child 7 Years old Female patient who experienced Occasional knee pain when walking (Knee pain), 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 26-FEB-2025.

The patient's medical history and current conditions included Precocious puberty.

Concomitant medications were not reported.

On 22-NOV-2024, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for Central precocious puberty (Lot numbers and Expiration dates not provided). On 25-JAN-2025, 2 months 4 days after the most recent dose of Eligard, the patient started experiencing occasional knee pain when walking which went away on its own and did not need analgesics. Corrective treatment was reported as none. Action taken with Eligard in response to the event was Dose Not Changed. De-challenge and re-challenge were Not applicable. The outcome of Knee pain was Not Recovered/ Not Resolved.

The reporter did not assess the seriousness or causality of the event in relationship to Eligard.

On 23-May-2025, follow up information was received by Adium via PSP Solutions (Patient Support Program) (reference number: NI-ADIUM-NI-0022-20250225), from consumer (non-healthcare professional) and sent to Tolmar on 26-May-2025. New information included: Added three new non-serious events of 'Nose and chin pimples' (Acne) and 'Pellets on hands and feet' (Skin disorder),'Eligard 22.5 mg every 3 months' (off label use). Narrative was updated.

On 22-Nov-2024, the patient began receiving Eligard 22.5 milligram, every 3 months via Subcutaneous route for Central precocious puberty as an off-label use. (Lot numbers and Expiration dates were not provided).

On an unknown date in May-2025, the patient experienced mild nose and chin pimples and mild pellets on hands and feet. No further information was 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.

The outcome of off label use was unknown, acne was not recovered, and skin disorder was recovering.

The reporter did not assess the seriousness of off label use, acne and skin disorder.

The reporter assessed the causality of the acne in relationship to Eligard and Eligard unspecified device as related.

The reporter did not provide the causality of off-label use and assessed the causality of skin disorder in relationship to Eligard and Eligard unspecified device as not related.

No further query was raised.

Listedness:
Acne>Eligard>Unlisted as per CCDS>07-Nov-2024
Acne>Eligard>Unlisted as per USPI>Feb-2025
Acne>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Acne>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Skin disorder>Eligard>Unlisted as per CCDS>07-Nov-2024
Skin disorder>Eligard>Unlisted as per USPI>Feb-2025
Skin disorder>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Skin disorder>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

Listedness of the events Knee pain is retained as per previous assessment.

Company Remarks (Sender's Comments) :

Continuation Sheet for CIOMS report

Evaluator comment (Tolmar): This is regarding 7 Years old female child patient who had Knee pain ('Occasional knee pain when walking'), Acne ('Nose and chin pimples') and Skin disorder ('Pellets on hands and feet') and off label use ('Eligard 22.5 mg every 3 months') during Eligard (leuprolide acetate) 22.5 mg therapy for precocious puberty. Tolmar assessed the event as non-serious since they do not meet the ICH seriousness criteria and are not IME events. The reported event Acne, Skin disorder were assessed as not related to Eligard (drug and device) considering the etiopathogenesis. Underlying precocious puberty is a contributing factor. The reported event off label use was assessed as not related to Eligard (drug and device) as the event occurred due to human action and not due to drug. Causality of the event Knee pain is retained as per previous assessment.

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) Asked but 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 : 22/Nov/2024 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) OCCASIONAL KNEE PAIN WHEN WALKING (Knee pain - 10023477, Arthralgia - 10003239)

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

2) Nose and chin pimples (Pimples - 10035049, Acne - 10000496)

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

3) Pellets on hands and feet (Skin disorder - 10040831, Skin disorder - 10040831)

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

4) Eligard 22.5 mg every 3 months (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) OCCASIONAL KNEE PAIN WHEN WALKING	
CORE	Labeled
2) Nose and chin pimples	
CORE	UnLabeled
3) Pellets on hands and feet	
CORE	UnLabeled
4) Eligard 22.5 mg every 3 months	
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
Route of Admin	:	1) Subcutaneous
Indications	:	1) Central Precocious Puberty [10073186 - Central precocious puberty]
Action(s) Taken With Drug	:	Not applicable

Causality

1) OCCASIONAL KNEE PAIN WHEN WALKING (Knee pain - 10023477, Arthralgia - 10003239)

Continuation Sheet for CIOMS report

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

2) Nose and chin pimples (Pimples - 10035049, Acne - 10000496)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Pellets on hands and feet (Skin disorder - 10040831, Skin disorder - 10040831)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Eligard 22.5 mg every 3 months (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) OCCASIONAL KNEE PAIN WHEN WALKING
CORE
2) Nose and chin pimples
CORE
3) Pellets on hands and feet
CORE
4) Eligard 22.5 mg every 3 months
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 milligram, q 3 month