SUSPECT ADVERSE REACTION REPORT

NI-TOLMAR, INC.-25NI057155

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
ASVA	NICARAGUA	25	Jan	2015	10	Female	25	Nov	2024

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

1) ACNE-LIKE PIMPLES ON HER FACE (Pimples (10035049), Acne (10000496))
(11/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing
2) feeling of heat and suffocation (Hot flush (10060800), Hot flush (10060800))
(16/May/2025 -) - Not Recovered/Not Resolved/Ongoing
3) sensation of heat (Sensation of heat (10039999), Feeling hot (10016334))
(16/May/2025 -) - Not Recovered/Not Resolved/Ongoing
4) Eligard 22.5 mg every 3 months (Off label use (10053762), Off label use (10053762))
(25/Nov/2024 -) - Unknown

Cont..

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) (25/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.-25NI057155
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
28/May/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
07/Jun/2025	☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) headache (Headache (10019211), Headache (10019211)(16/May/2025 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from NICARAGUA was received by Adium via Patient Support Program (reference number: NI-ADIUM-NI-0021-20250225) on 25-FEB-2025 from a Consumer/Other Non-Health Prof regarding a Child 10Year old Female patient who experienced Acne-like pimples on her face (Pimples), 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 30-FEB-2025.

The patient's medical history and current conditions included: Central Precocious Puberty.

Concomitant medications were not reported.

On 25-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 were not reported). On 11-FEB-2025, 2 months 18 days after the most recent dose of Eligard, the patient started with acne-like pimples on her face. Corrective treatment was not reported. Action taken with Eligard in response to the event was Dose Not Changed. De-challenge and re-challenge were Not Applicable. The outcome of Pimples was Not Recovered/Not Resolved.

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

On 28-May-2025 follow-up information from NICARAGUA was received by Adium via Patient Support Program (reference number: NI-ADIUM-NI-0021-20250225) from a Consumer (Non-Health Professional) and sent to Tolmar on 30-may-2025. New information included: Added new non-serious events of: "sensation of heat/Suffocation" (hot flush), "Sensation of heat" (Feeling hot), "Headache" (Headache) and ""Eligard 22.5 mg every 3 months" (Off label use).

On 25-NOV-2024, 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 reported) and experienced off-label use.

On 16-may-2025, the patient experienced sensation of heat, sensation of heat/ suffocation and mild headache. No further information was 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 hot flush, feeling hot and headache was not recovered and of off label use was unknown.

The reporter did not assess the seriousness of hot flush, feeling hot, off label use and headache.

The reporter did not provide the causality of hot flush, feeling hot, off label use and headache in relationship to Eligard and Eligard unspecified device.

No further query was raised.

Listedness

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

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

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

Sensation of heat>Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
Sensation of heat> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
Sensation of heat> Eligard®>unlisted as per USPI Eligard®>Feb-2025
Sensation of heat> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

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

Continuation Sheet for CIOMS report

Off label use> Eligard®>unlisted as per USPI Eligard®>Feb-2025
Off label use> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar): This is regarding a Child 10Year old Female patient who experienced Acne-like pimples on her face (Pimples), "sensation of heat/Suffocation" (hot flush), "Sensation of heat" (Feeling hot), "Headache" (Headache) and "'Eligard 22.5 mg every 3 months" (Off label use) during Eligard (Leuprolide acetate) 22.5 milligram therapy for Central Precocious Puberty. Tolmar assessed the reported events as non-serious since they did not meet the ICH seriousness criteria and are not IME events. The reported events of hot flush, feeling hot, acne and headache can be attributed to drug's initial stimulatory effect of the drug and not related to device. Event of off- label use us assessed as not suspected with drug and device as it is explained by human actions.

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

Causality

1) ACNE-LIKE PIMPLES ON HER FACE (Pimples - 10035049, Acne - 10000496)

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

2) feeling of heat and suffocation (Hot flush - 10060800, Hot flush - 10060800)

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

3) sensation of heat (Sensation of heat - 10039999, Feeling hot - 10016334)

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

4) Eligard 22.5 mg every 3 months (Off label use - 10053762, Off label use - 10053762)

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

5) headache (Headache - 10019211, Headache - 10019211)

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

Labeling :

1) ACNE-LIKE PIMPLES ON HER FACE	
CORE	UnLabeled
2) feeling of heat and suffocation	
CORE	UnLabeled
3) sensation of heat	
CORE	UnLabeled
4) Eligard 22.5 mg every 3 months	
CORE	UnLabeled
5) headache	
CORE	Labeled

Continuation Sheet for CIOMS report

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) ACNE-LIKE PIMPLES ON HER FACE (Pimples - 10035049, Acne - 10000496)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) feeling of heat and suffocation (Hot flush - 10060800, Hot flush - 10060800)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) sensation of heat (Sensation of heat - 10039999, Feeling hot - 10016334)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Eligard 22.5 mg every 3 months (Off label use - 10053762, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) 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) ACNE-LIKE PIMPLES ON HER FACE
CORE
2) feeling of heat and suffocation
CORE
CORE UnLabeled
3) sensation of heat
CORE
4) Eligard 22.5 mg every 3 months
CORE
5) headache
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 milligram, q 3 month

Drug 2 :Eligard® Unspecified Device

1) UNK