SUSPECT ADVERSE REACTION REPORT

NI-TOLMAR, INC.-24NI051233

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
SAAA	NICARAGUA	16	Nov	2016	7	Female	14	May	2024

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

1) Patient has been more altered than normal and in a bad mood (Mood altered (10027940), Mood altered (10027940))
Not Recovered/Not Resolved/Ongoing
2) Missed dose/Eligard was not administered in May due to availability (Delayed dose administration (10085266), Inappropriate schedule of product administration (10081572))
(/May/2025 -) - Unknown
3) Off-label use for non-approved indication/Eligard 22.5 mg was used for precocious puberty (Off label use in unapproved indication (10084345), Off label use (10053762))
(14/May/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)(14309A; 14310A; UNK)(22.5 Milligram, Injection)(Unknown)(22.5 Milligram, Injection)(Unknown)

Cont..

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
1) (22.5 milligram(s), 1 in 3 Month)	1) Subcutaneous
2) (22.5 milligram(s), 1 in 3 Month)	2) Subcutaneous

17. INDICATION(S) FOR USE

1) Precocious puberty [10058084 - Precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (14/May/2024 - 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) PRECOCIOUS PUBERTY (10058084, Precocious puberty) (Continuing: Yes)

Cont..

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, INC.-24NI051233
24c. DATE RECEIVED BY MANUFACTURER	**24d. REPORT SOURCE**
10/Jul/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	**25a. REPORT TYPE**
16/Jul/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 Patient Support Program ASOFARMA A TU LADO (reference number: NI-ADIUM-NI-0043-20240719) on 19-JUL-2024 from a Consumer/Other Non-Health Prof regarding a Child 7-Year-old Female patient who has been more altered than normal and in a bad mood (Mood altered) during Eligard (Leuprolide acetate) 22.5 milligram therapy for Precocious puberty. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 22-JUL-2024.

The patient's medical history and current conditions included Precocious puberty, Autism spectrum disorder and Genital haemorrhage.

Concomitant medications were not reported.

On 14-MAY-2024, the patient began receiving Eligard 22.5 milligram, q 3 month via Subcutaneous use for precocious puberty (Lot numbers: 14309A; 14310A; UNK; Expiration dates: OCT-2025; NOV-2025; UNK). On an unknown date, time to onset unknown after Eligard treatment was started, the patient had been more altered than normal and in a bad mood, since the patient was running around, screaming, talking very loudly, for this reason, she was more altered in the attitudes she normally used to have. At the end of July 2024, the patient should have bone plate exams of the hand and elbow bones, to check the bone density of the bones and a pelvic ultrasound.

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 Mood altered was Not Recovered/Not Resolved.

The reporter did not assess the seriousness of Mood altered and assessed the causality in relationship to Eligard as Not Reported.

On 10-Jul-2025, the follow up from Nicaragua by Adium via Patient Support Program ASOFARMA A TU LADO (Reference number: NI-ADIUM-NI-0043-20240719) and sent to Tolmar on 10-Jul-2025. New information included: Updated the patient's weight, added new dosage regimen of Eligard, added new non-serious events of "Off-label use for non-approved indication/Eligard 22.5 mg was used for precocious puberty" (Off label use) and "Missed dose/Eligard was not administered in May due to availability" (inappropriate schedule of product administration) and narrative was updated.

On an unknown date in May-2025, the patient was intended to receive Eligard (leuprolide acetate) 22.5 mg, every 3 months via subcutaneous route for precocious puberty (Lot numbers and Expiration dates were not provided).

On an unknown date in May-2025, Eligard was not administered in due to availability (May-2025) and was given medication from another laboratory. No further details were provided.

Corrective treatment was not reported.

Action taken with Eligard in response to events off label use and inappropriate schedule of product administration was unknown. De-challenge and re-challenge were not applicable.

The outcome of the events inappropriate schedule of product administration and off label use was unknown

The reporter did not assess the seriousness of the events inappropriate schedule of product administration and off label use.

The reporter provided the causality of the event inappropriate schedule of product administration as not related in relationship to Eligard and Eligard unspecified device.

The reporter did not provide the causality of the event off label use in relationship to Eligard and Eligard unspecified device.

No further query was raised.

Listedness of previously reported event mood altered was retained as previously assessed.

inappropriate schedule of product administration>Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
inappropriate schedule of product administration> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
inappropriate schedule of product administration> Eligard®>unlisted as per USPI Eligard®>Feb-2025
inappropriate schedule of product administration> 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
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) :

Continuation Sheet for CIOMS report

Evaluator comment (Tolmar):
Causality of previously reported events were retained as previously assessed.
mood altered: not related to drug and device.

This is regarding a child 7-year-old female patient who reported Off label use (Off-label use for non-approved indication/Eligard 22.5 mg was used for precocious puberty) and inappropriate schedule of product administration (Missed dose/Eligard was not administered in May due to availability) during Eligard(leuprolide acetate) 22.5mg therapy for prostate cancer. Tolmar assessed the reported events as non-serious since they did not meet the ICH seriousness criteria. The causality of events inappropriate schedule of product administration and off label use was assessed as not related to suspect Eligard(drug and device) as the events occurred with the product due to human action rather than due to 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
		2) 22.5 Milligram
		3) 22.5 Milligram
Form of Admin	:	1) Injection
		2) Injection
		3) Injection
Lot Number	:	1) 14309A; 14310A; UNK
		2) Unknown
		3) Unknown
Daily Dose	:	(22.5 milligram(s), 1 in 3 Month)
		(22.5 milligram(s), 1 in 3 Month)
		(22.5 milligram(s), 1 in 3 Month)
Route of Admin	:	1) Subcutaneous
		2) Subcutaneous
		3) Subcutaneous
Indications	:	1) Precocious puberty [10058084 - Precocious puberty]
Therapy Dates	:	1) From : 14/May/2024 To :Unknown
		2) From : /May/2025 To :Unknown
Action(s) Taken With Drug	:	Unknown

Causality

1) Patient has been more altered than normal and in a bad mood (Mood altered - 10027940, Mood altered - 10027940)

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

2) Missed dose/Eligard was not administered in May due to availability (Delayed dose administration - 10085266, Inappropriate schedule of product administration - 10081572)

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

3) Off-label use for non-approved indication/Eligard 22.5 mg was used for precocious puberty (Off label use in unapproved indication - 10084345, Off label use - 10053762)

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

Labeling :

1) Patient has been more altered than normal and in a bad mood
   CORE UnLabeled
2) Missed dose/Eligard was not administered in May due to availability
   CORE UnLabeled
3) Off-label use for non-approved indication/Eligard 22.5 mg was used for precocious puberty
   CORE UnLabeled

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
2) Injection
3) Injection
Lot Number : 1) 14309A; 14310A; UNK
2) Unknown
3) Unknown
Route of Admin : 1) Subcutaneous
2) Subcutaneous
3) Subcutaneous
Indications : 1) Precocious puberty [10058084 - Precocious puberty]
Therapy Dates : 1) From : 14/May/2024 To :Not applicable
2) From : /May/2025 To :Not applicable
Action(s) Taken With Drug : Not applicable

Causality

1) Patient has been more altered than normal and in a bad mood (Mood altered - 10027940, Mood altered - 10027940)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Missed dose/Eligard was not administered in May due to availability (Delayed dose administration - 10085266, Inappropriate schedule of product administration - 10081572)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Off-label use for non-approved indication/Eligard 22.5 mg was used for precocious puberty (Off label use in unapproved indication - 10084345, Off label use - 10053762)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Patient has been more altered than normal and in a bad mood
CORE
2) Missed dose/Eligard was not administered in May due to availability
CORE
3) Off-label use for non-approved indication/Eligard 22.5 mg was used for precocious puberty
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 22.5 milligram, q 3 month Expiration dates: OCT-2025; NOV-2025; UNK

2) This dose was not administered

3) Replacement dose given

Drug 2 :Eligard® Unspecified Device

1) 22.5 milligram, q 3 month Expiration dates: OCT-2025; NOV-2025; UNK

2) This dose was not administered

3) Replacement dose given

23. OTHER RELEVANT HISTORY (Continuation...)

2) AUTISM (10003805 , Autism) (Continuing : YES)

3) 1 BLEEDING TWICE IN 1 DAY (10071812 , Genital bleeding) (Continuing : NO)