

SUSPECT ADVERSE REACTION REPORT NI-TOLMAR, INC.-25NI056860												

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last) KAPJ	1a. COUNTRY NICARAGUA	2. DATE OF BIRTH			2a. AGE Years 6	3. SEX Female	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION <input type="checkbox"/> PATIENT DIED <input type="checkbox"/> LIFE THREATENING <input type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION <input type="checkbox"/> RESULTS IN PERSISTENCE OR SIGNIFICANT DISABILITY/INCAPACITY <input type="checkbox"/> CONGENITAL ANOMALY <input type="checkbox"/> OTHER MEDICALLY IMPORTANT CONDITION
		Day 01	Month Sep	Year 2018			Day	Month Nov	Year 2024	
7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) 1) SENSITIVITY TO THE ENVIRONMENT (Sensory processing sensitivity (10087492), Sensory processing sensitivity (10087492)) (/Nov/2024 -) - Recovering/Resolving 2) FEELING WARMTH/FEELING TOO HOT (Feeling of warmth (10016357), Feeling hot (10016334)) (/Nov/2024 -) - Recovering/Resolving 3) Feeling of suffocation (Chest discomfort (10008469), Chest discomfort (10008469)) (24/Feb/2025 -) - Recovered/Resolved 4) PATIENT WAS USING 22.5 MG FOR CENTRAL PRECOCIOUS PUBERTY (Off label dosing (10074165), Off label use (10053762)) (08/Nov/2024 -) - Unknown										

Cont..

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S)(include generic name) 1) Eligard® (Leuprolide acetate, Leuprolide acetate) (Suspect) (Injection)(Unknown)		20. DID EVENT ABATE AFTER STOPPING DRUG? <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA 21. DID EVENT REAPPEAR AFTER REINTRODUCTION <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA (NA : Not Applicable)
15. DAILY DOSE(S) 1) (22.5 milligram(s), 1 in 3 Month)	16. ROUTE(S) OF ADMINISTRATION 1) Subcutaneous	
17. INDICATION(S) FOR USE 1) Central Precocious Puberty [10073186 - Central precocious puberty]		
18. THERAPY DATE(S) (from/to) (08-Nov-2024 - Ongoing)	19. THERAPY DURATION	

Cont..

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction) 1) LAMOTRIGINA(LAMOTRIGINE)	Cont..
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) 1) LENNOX-GASTAUT SYNDROME (10048816, Lennox-Gastaut syndrome) (/Jun/2020 -) (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 <input type="checkbox"/> YES <input type="checkbox"/> NO	24b. MFR CONTROL NO. NI-TOLMAR, INC.-25NI056860	
24c. DATE RECEIVED BY MANUFACTURER 05/Jun/2025	24d. REPORT SOURCE <input checked="" type="checkbox"/> STUDY <input type="checkbox"/> LITERATURE <input type="checkbox"/> HEALTH PROFESSIONAL	
DATE OF THIS REPORT 15/Jul/2025	25a. REPORT TYPE <input type="checkbox"/> INITIAL <input checked="" type="checkbox"/> FOLLOWUP	

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) DID NOT WANT TO EAT (Appetite lost (10003028), Decreased appetite (10061428)/(Nov/2024 -) - Recovering/Resolving)

6) CRIES FOR EVERYTHING AND FOR NO REASON (Crying (10011469), Crying (10011469)/(Nov/2024 -) - Recovered/Resolved)

7) IRRITABLE AND HATEFUL (Irritability (10022998), Irritability (10022998)/(Nov/2024 -) - Recovering/Resolving)

8) DEPRESSED/FELT SAD AND DID NOT WANT TO LEAVE THE ROOM, DID NOT WANT TO TAKE A BATH (Depressed mood (10012374), Depressed mood (10012374)/(Nov/2024 -) - Recovering/Resolving)

9) Hot flashes (Hot flashes (10020407), Hot flush (10060800)(24/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

10) SWEATING (Sweating (10042661), Hyperhidrosis (10020642)/(Nov/2024 -) - Recovering/Resolving)

11) Sudden urge to cry (Crying (10011469), Crying (10011469)(24/Feb/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-0014-20250212) on 12-FEB-2025 from a Consumer/Other Non-Health Professional regarding a Child 6 Years old Female patient who experienced Sensitivity to the environment (Sensory processing sensitivity), Feeling warmth (Feeling hot), cries for everything and for no reason (Crying), Did not want to eat (Appetite lost), Irritable and hateful (Irritability), Depressed/felt sad and did not want to leave the room, did not want to take a bath (Feeling of warmth), Sweating (Sweating), 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 17-FEB-2025.

The patient's medical history and current conditions included: Precocious puberty, Autism spectrum disorder, Lennox-Gastaut syndrome.

Concomitant medications included: LAMOTRIGINA, LEVETIRACETAM and RIVOTRIL.

On 08-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 an unknown date in NOV-2024, two or three weeks after the most recent dose of Eligard, the patient experienced becoming sensitive to the environment, sometimes irritable and hateful. Additionally, the patient experienced being depressed as she did not want to eat, did not want to leave the room, did not want to take a bath, cried about everything for no reason, she felt sad. Also, in NOV-2024, on occasions; the patient felt warmth, which was associated with sweating.

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 Sensory processing sensitivity, feeling of warmth, crying, appetite lost, irritability, depressed mood and sweating was recovering.

The reporter did not assess the seriousness or causality of the events in relationship to Eligard and Eligard unspecified device.

On 07-May-2025, follow-up information was received by Adium via Patient Support Program (reference number: NI-ADIUM-NI-0014-20250212) from a consumer (non-healthcare professional). New information included: Added four non-serious events of "Hot flashes" (Hot flush), "Patient was using 22.5 mg for Central Precocious Puberty" (Off label use), "Choking" (Choking) and "Sudden urge to cry" (Crying). Added two concomitant medications: Topiramate and Valproic acid. Updated verbatim of events from "Feeling warmth" to "Feeling warmth/Feeling too hot" and from "Cries for everything and for no reason" to "Cries for everything and for no reason, Sudden urge to cry". No further information was available. The report was sent to Tolmar on 09-May-2025.

Concomitant medications were Topiramate and Valproic Acid for the indication Lennox Gastaut Syndrome with which patient experienced nausea and vomiting and thrombocytopenia respectively.

On 08-NOV-2024, the patient began receiving Eligard 22.5 milligram, q 3 month, via Subcutaneous use for Central precocious puberty (Off label use) (Lot numbers and Expiration dates were not reported).

On an unknown date, the patient experienced choking and felt too hot and wanted to take off clothes.

On 24-Feb-2025, the patient experienced hot flashes and sudden urge to cry.

Corrective treatment was not provided.

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 was recovered.

Continuation Sheet for CIOMS report

The outcome of choking was unknown.

The outcome of feeling hot and crying was not recovered.

The reporter did not assess seriousness of hot flush, choking, feeling hot and crying.

The reporter did not provide causality of choking, feeling hot and crying in relationship to Eligard and Eligard unspecified device.

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

No further queries were raised.

On 05-Jun-2025, the follow up was received by Adium via Patient Support Program (reference number: NI-ADIUM-NI-0014-20250212) and sent to tolmar on 05-Jun-2025. New information included: A new non-serious event of "Feeling of suffocation" (Chest discomfort) was added.

On 24-Feb-2025, the patient experienced the feeling of suffocation due to hot flashes. No further details were reported.

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 chest discomfort was recovered.

The reporter did not assess seriousness of chest discomfort.

The reporter did not provide causality of chest discomfort in relationship to Eligard and Eligard unspecified device.

Listedness:

Labelling of previously reported events retained as per previous assessment.

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

Crying>Eligard>listed as per CCDS>07-Nov-2024

Crying>Eligard>Unlisted as per USPI>Feb-2025

Crying>Eligard unspecified device>Unlisted as per USPI>Feb-2025

Crying>Eligard>listed as per Canadian monograph>02-Apr-2025

Hot flush>Eligard>listed as per CCDS>07-Nov-2024

Hot flush>Eligard>Unlisted as per USPI>Feb-2025

Hot flush>Eligard unspecified device>Unlisted as per USPI>Feb-2025

Hot flush>Eligard>listed as per Canadian monograph>02-Apr-2025

Chest discomfort>Eligard>Unlisted as per CCDS>07-Nov-2024

Chest discomfort>Eligard>Unlisted as per USPI>Feb-2025

Chest discomfort>Eligard unspecified device>Unlisted as per USPI>Feb-2025

Chest discomfort>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Causality of previously reported events retained as per previous assessment:

Evaluator comment (Tolmar): This is regarding a Child 6 Years old Female patient who experienced Sensory processing sensitivity (Sensitivity to the environment), Feeling hot (FEELING WARMTH/FEELING TOO HOT), Crying (cries for everything and for no reason) , decreased appetite (Did not want to eat), Irritability (Irritable and hateful) , Depressed mood (felt sad and did not want to leave the room), Sweating (Sweating), Off label use (the patient began receiving Eligard 22.5 milligram, q 3 month, via Subcutaneous use for Central precocious puberty), hot flush(Hot flashes), crying(Sudden urge to cry) and chest discomfort (feeling of suffocation) during Eligard (Leuprolide acetate) 22.5 milligram therapy for Central precocious puberty. Tolmar assessed the reported events as non-serious since there was no information suggesting any intervention or medical treatment for the reported events. Tolmar assessed crying, decreased appetite, irritability, crying, hyperhidrosis, depressed mood, hot flush as related to Eligard drug based on product safety profile. Sensory processing sensitivity, feeling hot and chest discomfort were assessed as not related to Eligard drug based on inconsistent safety profile. The causality of the 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. All the reported events were assessed as not related to device component of the drug based on the case information.

14.SUSPECT DRUG(S) (Continuation...)

Continuation Sheet for CIOMS report

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]
 Action(s) Taken With Drug : Dose not changed

Causality

- 1) SENSITIVITY TO THE ENVIRONMENT (Sensory processing sensitivity - 10087492, Sensory processing sensitivity - 10087492)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 2) FEELING WARMTH/FEELING TOO HOT (Feeling of warmth - 10016357, Feeling hot - 10016334)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 3) Feeling of suffocation (Chest discomfort - 10008469, Chest discomfort - 10008469)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 4) PATIENT WAS USING 22.5 MG 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
- 5) DID NOT WANT TO EAT (Appetite lost - 10003028, Decreased appetite - 10061428)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 6) CRIES FOR EVERYTHING AND FOR NO REASON (Crying - 10011469, Crying - 10011469)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 7) IRRITABLE AND HATEFUL (Irritability - 10022998, Irritability - 10022998)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 8) DEPRESSED/ FELT SAD AND DID NOT WANT TO LEAVE THE ROOM, DID NOT WANT TO TAKE A BATH (Depressed mood - 10012374, Depressed mood - 10012374)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 9) Hot flashes (Hot flashes - 10020407, Hot flush - 10060800)
 Causality as per reporter : Related
 Causality as per Mfr : Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 10) SWEATING (Sweating - 10042661, Hyperhidrosis - 10020642)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 11) Sudden urge to cry (Crying - 10011469, Crying - 10011469)

Continuation Sheet for CIOMS report

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

Labeling :

- 1) SENSITIVITY TO THE ENVIRONMENT
 CORE UnLabeled
- 2) FEELING WARMTH/FEELING TOO HOT
 CORE UnLabeled
- 3) Feeling of suffocation
 CORE UnLabeled
- 4) PATIENT WAS USING 22.5 MG FOR CENTRAL PRECOCIOUS PUBERTY
 CORE UnLabeled
- 5) DID NOT WANT TO EAT
 CORE Labeled
- 6) CRIES FOR EVERYTHING AND FOR NO REASON
 CORE Labeled
- 7) IRRITABLE AND HATEFUL
 CORE Labeled
- 8) DEPRESSED/ FELT SAD AND DID NOT WANT TO LEAVE THE ROOM, DID NOT WANT TO TAKE A BATH
 CORE Labeled
- 9) Hot flashes
 CORE Labeled
- 10) SWEATING
 CORE Labeled
- 11) Sudden urge to cry
 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
 Route of Admin : 1) Subcutaneous
 Indications : 1) Central Precocious Puberty [10073186 - Central precocious puberty]
 Action(s) Taken With Drug : Not applicable

Causality

- 1) SENSITIVITY TO THE ENVIRONMENT (Sensory processing sensitivity - 10087492, Sensory processing sensitivity - 10087492)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 2) FEELING WARMTH/FEELING TOO HOT (Feeling of warmth - 10016357, Feeling hot - 10016334)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 3) Feeling of suffocation (Chest discomfort - 10008469, Chest discomfort - 10008469)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
- 4) PATIENT WAS USING 22.5 MG 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
- 5) DID NOT WANT TO EAT (Appetite lost - 10003028, Decreased appetite - 10061428)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 6) CRIES FOR EVERYTHING AND FOR NO REASON (Crying - 10011469, Crying - 10011469)
 Causality as per reporter : Not Reported
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable

Continuation Sheet for CIOMS report

7) IRRITABLE AND HATEFUL (Irritability - 10022998, Irritability - 10022998)

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

8) DEPRESSED/FELT SAD AND DID NOT WANT TO LEAVE THE ROOM, DID NOT WANT TO TAKE A BATH (Depressed mood - 10012374, Depressed mood - 10012374)

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

9) Hot flashes (Hot flashes - 10020407, Hot flush - 10060800)

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

10) SWEATING (Sweating - 10042661, Hyperhidrosis - 10020642)

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

11) Sudden urge to cry (Crying - 10011469, Crying - 10011469)

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

Labeling :

- 1) SENSITIVITY TO THE ENVIRONMENT
CORE
- 2) FEELING WARMTH/FEELING TOO HOT
CORE
- 3) Feeling of suffocation
CORE
- 4) PATIENT WAS USING 22.5 MG FOR CENTRAL PRECOCIOUS PUBERTY
CORE
- 5) DID NOT WANT TO EAT
CORE
- 6) CRIES FOR EVERYTHING AND FOR NO REASON
CORE
- 7) IRRITABLE AND HATEFUL
CORE
- 8) DEPRESSED/FELT SAD AND DID NOT WANT TO LEAVE THE ROOM, DID NOT WANT TO TAKE A BATH
CORE
- 9) Hot flashes
CORE
- 10) SWEATING
CORE
- 11) Sudden urge to cry
CORE

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

Dosage Text :

Drug 1 :Eligard®

- 1) 22.5 milligram, q 3 month

22. CONCOMITANT DRUG(S) (Continuation...)

1). Drug	:	LAMOTRIGINA
Active Substance	:	1) LAMOTRIGINE
Form Strength	:	
Indications	:	1) Product used for unknown indication [10070592 - Product used for unknown indication]
Dosage Text	:	1) 75 mg every 12 hours

Continuation Sheet for CIOMS report

2). Drug : LEVETIRACETAM
 Active Substance : 1) LEVETIRACETAM
 Form Strength :
 Indications : 1) Product used for unknown indication [10070592 - Product used for unknown indication]
 Dosage Text : 1) 5 mg every 12 hours.

3). Drug : RIVOTRIL
 Active Substance : 1) CLONAZEPAM
 Form Strength :
 Indications : 1) Product used for unknown indication [10070592 - Product used for unknown indication]
 Dosage Text : 1) 2.5 mg/ml 12 drops at night

4). Drug : TOPIRAMATE
 Active Substance : 1) TOPIRAMATE
 Form Strength :
 Indications : 1) Lennox Gastaut Syndrome [10048816 - Lennox-Gastaut syndrome]
 Therapy Dates : 1) From : /Jun/2020 To :

5). Drug : VALPROIC ACID
 Active Substance : 1) VALPROIC ACID
 Form Strength :
 Indications : 1) Lennox Gastaut Syndrome [10048816 - Lennox-Gastaut syndrome]
 Therapy Dates : 1) From : /Jun/2020 To :

23. OTHER RELEVANT HISTORY (Continuation...)

- 2) AUTISM GRADE 2 (10063844 , Autism spectrum disorder) (/Oct/2020 -) (Continuing : YES)
 3) NAUSEA (10028813 , Nausea) (/Oct/2020 -) (Continuing : YES)
 4) VOMITING (10047700 , Vomiting) (/Oct/2020 -) (Continuing : YES)
 5) CENTRAL PRECOCIOUS PUBERTY (10073186 , Central precocious puberty) (Continuing : YES)