SUSPECT ADVERSE REACTION REPORT

HN-TOLMAR, INC.-23HN042508

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
EGTC	HONDURAS	16	Jul	2015	8	Female	04	Aug	2023

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

1) MOOD SWINGS (Mood swings (10027951), Mood swings (10027951))
(04/Aug/2023 -) - Not Recovered/Not Resolved/Ongoing
2) HAD CRYING CRISES, EPISODES OF SUDDEN CRYING (Crying (10011469), Crying (10011469))
(04/Aug/2023 -) - Not Recovered/Not Resolved/Ongoing
3) FEELING ANXIOUS AT NIGHT (Anxiety (10002855), Anxiety (10002855))
(04/Aug/2023 -) - Recovered/Resolved
4) Burning sensation in the throat (Throat burning sensation of (10043514), Throat irritation (10043521))
(16/Jun/2025 -) - Recovering/Resolving

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)(Unknown)

Cont..

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☑ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
1) (45 milligram(s), 1 in 6 Month)	1) Subcutaneous
2) (45 milligram(s), 1 in 6 Month)	2) Subcutaneous

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ NA

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Precocious puberty [10058084 - Precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (19/Jul/2023 - 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) PRECOCIOUS PUBERTY (10058084, 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	HN-TOLMAR, INC.-23HN042508
24c. DATE RECEIVED BY MANUFACTURER: 16/Jun/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 23/Jun/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...)

5) EXACERBATION OF RHINITIS WITH ADENOID INFLAMMATION (Allergic rhinitis (10001723), Rhinitis allergic (10039085) - Unknown)

6) HEADACHE, IN THE FRONTAL REGION, OF MODERATE PULSATING INTENSITY (Headache (10019211), Headache (10019211)(08/Jan/2024 -) - Recovered/Resolved)

7) FEELS SAD (Feeling sad (10016364), Depressed mood (10012374)(04/Aug/2023 -) - Recovered/Resolved)

8) REDNESS AT THE APPLICATION SITE (Injection site redness (10022098), Injection site erythema (10022061)(08/Jan/2024 -) - Not Recovered/Not Resolved/Ongoing)

9) PAIN IN THE AREA OF APPLICATION (Injection site pain (10022086), Injection site pain (10022086)(08/Jan/2024 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from HONDURAS was received by Adium (reference number: HN-2614-20230809) on 08-AUG-2023 from a Consumer/Other Non-Health Prof regarding a Child 8 Years old Female patient who experienced Mood swings (Mood swings), Had crying crises, episodes of sudden crying (Crying), Feeling anxious at night (Anxiety), Feels sad (Feeling sad), during Eligard (Leuprolide acetate) 45 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 09-AUG-2023.

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

Concomitant medications were not reported.

On 19-JUL-2023, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for Precocious puberty (Batch details were not provided). On 04-AUG-2023, the patient started to had mood swings at times she felt sad and had crying crises, episodes of sudden crying and was feeling anxious at night.

Corrective treatment was not reported. No further details were 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 Mood swings was Not Recovered. The outcome of Crying was Not Recovered. The outcome of Anxiety was Not Recovered. The outcome of Feeling sad was Not Recovered.

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

On 13-Feb-2024, follow up information was received from a Consumer/Other Non-Healthcare Professional and sent to Tolmar on 14-FEB-2024. New information included non-serious events of Headache (Headache) exacerbation of rhinitis with adenoid inflammation (Allergic rhinitis), details of previously reported events of feeling sad, anxiety and case course details.

On 08-JAN-2024, after the most recent dose of Eligard, the patient experienced headache in the frontal region, of moderate pulsating intensity, without fever. The pain improved with over-the-counter medication Acetaminophen, and the patient was currently recovered from the headache. However, on an unspecified date experienced an exacerbation of rhinitis with adenoid inflammation was reported. The patient recovered from the previously reported episodes of sadness and anxiety. No further details were provided.

Corrective treatment included ACETAMINOPHEN.

Action taken with Eligard in response to the events was Dose Not Changed. De-challenge was Not applicable, and re-challenge was Not applicable.

The outcome of Anxiety was Recovered. The outcome of Headache was Recovered. The outcome of Allergic rhinitis was Unknown. The outcome of Feeling sad was Recovered.

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

On 24-APR-2024, follow-up information was received by Adium (reference number: HN-2614-20230809) from a Consumer/Other Non-Health Prof and sent to Tolmar on 24-APR-2024. New information included details regarding the events Injection site redness and Injection site pain. Added most recent Eligard dose.

On 30-DEC-2023, the patient received Eligard 45 milligram, q 6 month via Subcutaneous use (Lot numbers and Expiration dates were not provided). On 08-JAN-2024, the patient experienced redness at the application site and pain in the area of application. Reportedly, the patient hit the buttocks area and then presented this symptom.

Corrective treatment was not reported.

Continuation Sheet for CIOMS report

Action taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were not applicable.

The outcome of Injection site redness was Not Recovered. The outcome of Injection site pain was Not Recovered.

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

On 16-Jun-2025, the follow up information was received by Adium (reference number: HN-2614-20230809) from a Consumer/Other Non-Health Prof and sent to Tolmar on 17-Jun-2024. New information included a new non-serious event of "Burning sensation in the throat" (throat irritation) was added.

On 16-Jun-2025, the patient's family reported that the patient experienced burning in the tonsils. No further information reported.

Corrective treatment for throat irritation was Acetaminophen 500mg orally every 12 hours as indicated by doctor.

Action taken with Eligard in response to the event was dose not changed. De-challenge and re-challenge were not applicable.

The outcome of throat irritation was recovering.

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

No further information is expected as the reporter did not consent to be contacted for follow-up.

Listedness of previously reported events mood swings, crying, anxiety, allergic rhinitis, headache, depressed mood, injection site erythema, injection site pain was retained as previously assessed.
Throat irritation >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
Throat irritation > Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
Throat irritation > Eligard®>unlisted as per USPI Eligard®>Feb-2025
Throat irritation > Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Evaluator comment (Tolmar):

Causality of previously reported events were retained as previously assessed.
mood swings: not related to drug and device
crying: not related to drug and device
anxiety: not related to drug and device
allergic rhinitis: not related to drug and device
headache: not related to drug and device
depressed mood: related to drug and not related to device
injection site erythema: related to drug and device
injection site pain: related to drug and device

FU added event of throat irritation (burning sensation in throat). Tolmar assessed the reported event as non-serious since it did not meet the ICH seriousness criteria. The causality of event throat irritation was assessed as not related to suspect Eligard(drug and device) considering the nature of event, inconsistency with the safety profile of the drug.

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
		2) Injection
Lot Number	:	1) Unknown
		2) Unknown
Daily Dose	:	(45 milligram(s), 1 in 6 Month)
		(45 milligram(s), 1 in 6 Month)
Route of Admin	:	1) Subcutaneous
		2) Subcutaneous
Indications	:	1) Precocious puberty [10058084 - Precocious puberty]
Therapy Dates	:	1) From : 19/Jul/2023 To :Continuing
		2) From : 30/Dec/2023 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Continuation Sheet for CIOMS report

Causality

1) MOOD SWINGS (Mood swings - 10027951, Mood swings - 10027951)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) HAD CRYING CRISES, EPISODES OF SUDDEN CRYING (Crying - 10011469, Crying - 10011469)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) FEELING ANXIOUS AT NIGHT (Anxiety - 10002855, Anxiety - 10002855)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Burning sensation in the throat (Throat burning sensation of - 10043514, Throat irritation - 10043521)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) EXACERBATION OF RHINITIS WITH ADENOID INFLAMMATION (Allergic rhinitis - 10001723, Rhinitis allergic - 10039085)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) HEADACHE, IN THE FRONTAL REGION, OF MODERATE PULSATING INTENSITY (Headache - 10019211, Headache - 10019211)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) FEELS SAD (Feeling sad - 10016364, Depressed mood - 10012374)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

8) REDNESS AT THE APPLICATION SITE (Injection site redness - 10022098, Injection site erythema - 10022061)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

9) PAIN IN THE AREA OF APPLICATION (Injection site pain - 10022086, Injection site pain - 10022086)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) MOOD SWINGS
CORE UnLabeled

2) HAD CRYING CRISES, EPISODES OF SUDDEN CRYING
CORE UnLabeled

3) FEELING ANXIOUS AT NIGHT
CORE UnLabeled

4) Burning sensation in the throat
CORE UnLabeled

5) EXACERBATION OF RHINITIS WITH ADENOID INFLAMMATION
CORE UnLabeled

6) HEADACHE, IN THE FRONTAL REGION, OF MODERATE PULSATING INTENSITY
CORE Labeled

7) FEELS SAD
CORE Labeled

8) REDNESS AT THE APPLICATION SITE
CORE UnLabeled

9) PAIN IN THE AREA OF APPLICATION

Continuation Sheet for CIOMS report

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
Indications : 1) Precocious puberty [10058084 - Precocious puberty]
Action(s) Taken With Drug : Not applicable

Causality

1) MOOD SWINGS (Mood swings - 10027951, Mood swings - 10027951)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) HAD CRYING CRISES, EPISODES OF SUDDEN CRYING (Crying - 10011469, Crying - 10011469)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) FEELING ANXIOUS AT NIGHT (Anxiety - 10002855, Anxiety - 10002855)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Burning sensation in the throat (Throat burning sensation of - 10043514, Throat irritation - 10043521)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) EXACERBATION OF RHINITIS WITH ADENOID INFLAMMATION (Allergic rhinitis - 10001723, Rhinitis allergic - 10039085)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) HEADACHE, IN THE FRONTAL REGION, OF MODERATE PULSATING INTENSITY (Headache - 10019211, Headache - 10019211)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) FEELS SAD (Feeling sad - 10016364, Depressed mood - 10012374)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

8) REDNESS AT THE APPLICATION SITE (Injection site redness - 10022098, Injection site erythema - 10022061)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

9) PAIN IN THE AREA OF APPLICATION (Injection site pain - 10022086, Injection site pain - 10022086)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) MOOD SWINGS
CORE
2) HAD CRYING CRISES, EPISODES OF SUDDEN CRYING
CORE
3) FEELING ANXIOUS AT NIGHT
CORE
4) Burning sensation in the throat
CORE

Continuation Sheet for CIOMS report

5) EXACERBATION OF RHINITIS WITH ADENOID INFLAMMATION
CORE
6) HEADACHE, IN THE FRONTAL REGION, OF MODERATE PULSATING INTENSITY
CORE
7) FEELS SAD
CORE
8) REDNESS AT THE APPLICATION SITE
CORE
9) PAIN IN THE AREA OF APPLICATION
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

2) 45 milligram, q 6 month