SUSPECT ADVERSE REACTION REPORT

HN-TOLMAR, INC.-23HN041972

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
SMAO	HONDURAS	09	Jun	2015	8	Female	10	Jan	2025

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

1) Growth was a little advanced (Growth accelerated (10018746), Growth accelerated (10018746))
Recovered/Resolved
2) Completion of treatment (Therapy cessation (10065154), Therapy cessation (10065154))
(10/Jan/2025 -) - 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) (45 Milligram, Injection)(Unknown)

Cont..

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

15. DAILY DOSE(S)

1) (45 milligram(s), 1 in 6 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) Precocious puberty [10058084 - Precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (31/Oct/2022 - 10/Jan/2025)	

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.-23HN041972
24c. DATE RECEIVED BY MANUFACTURER: 25/Aug/2025	24d. REPORT SOURCE: ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 27/Aug/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...)

Event Description :

This Study report from HONDURAS was received by Adium (reference number: HN-2578-20230714) on 14-JUL-2023 from a Consumer regarding a Child 8 Years old Female patient who experienced Growth was a little advanced (Growth accelerated) during Eligard (Leuprolide acetate) 45 milligram therapy for precocious puberty. The report was sent to Tolmar on 14-JUL-2023. The needle component of the constituent device was not identified in the report.

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

Concomitant medications were not reported.

On an unspecified date the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for precocious puberty (Lot numbers and Expiration dates not provided). Reportedly, the patient had no longer bad odor in the armpits which she had before starting treatment with Eligard. On an unspecified date, unknown time after the most recent dose of Eligard a bone age test was performed to study the growth of the bones and skin, and the doctor commented that the growth was a little advanced. On an unspecified date, she had more tests, the names were unknown, but the results were normal. If the patient was going to continue with Eligard treatment was unknown because she had not yet had an appointment with the pediatrician and did not know if he was going to prescribe more applications. Corrective treatment was not reported. Action taken with Eligard in response to the events was Unknown. De-challenge was not applicable, and re-challenge was not applicable. The outcome of Growth accelerated was Recovered/Resolved.

Relevant test results included:

Unknown date: Bone formation test: growth was a little advanced (Ref range: Not provided)

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

On 25-Aug-2025, the follow up information was received by Adium (reference number: HN-2578-20230714 (1)) from a Consumer (other non-health professional) and sent to Tolmar on 26-Aug-2025. New information included: Added new non-serious event of "completion of treatment" (therapy cessation). Added the therapy start and end date. Narrative was updated.

On 31-Oct-2022, the patient began receiving Eligard 45 milligram, q 6 month via subcutaneous use for precocious puberty (Lot numbers and Expiration dates not provided).

On 10-Jan-2025, the patient's therapy was ceased. No further information was provided.

Corrective treatment was unknown.

Action taken with Eligard in response to the event was unknown. De-challenge was not applicable, and re-challenge was not applicable.

The outcome of therapy cessation was unknown.

The reporter did not assess the seriousness of therapy cessation.

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

No further queries were raised.

Listedness of previously reported event growth accelerated was retained as previously assessed.
therapy cessation >Eligard® >unlisted as per CCDS Eligard®> 7-Nov-2024
therapy cessation> Eligard® >unlisted as per Canadian Monograph Eligard®> 2-Apr-2025
therapy cessation> Eligard®>unlisted as per USPI Eligard®>Feb-2025
therapy cessation> Eligard® Unspecified Device>unlisted as per USPI Eligard®>Feb-2025

Company Remarks (Sender's Comments) :

Evaluator Comment (Tolmar): This 8 years old female patient experienced Growth accelerated (Growth was a little advanced) during Eligard (Leuprolide acetate) 45 milligram therapy for precocious puberty. Tolmar assessed Growth accelerated as serious due to medically significant in line with reporter's assessment. Growth accelerated was assessed as not related to Eligard (drug and device) based on the case context and inconsistency of the events with the product safety profile.

FU added event therapy cessation (completion of treatment). Tolmar assessed the reported event as non-serious since it did not meet the ICH seriousness criteria. The causality of event therapy cessation 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 drug.

Continuation Sheet for CIOMS report

Additional Information (Continuation...)

Lab Result :

Test Name	Test Date	Test Result	Normal Value
BONE AGE TEST	Unknown		

Test Result (Code) / Result Unstructured Data (free text) :

1) Test Name: BONE AGE TEST

Result Unstructured Data (free text) : Notes: Growth was a little advanced (growth accelerated).

Test Date: Unknown

Lab Comments :

1) Test Name : BONE AGE TEST

Lab Comments : Growth was a little advanced (growth accelerated).

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

Product-Reaction Level

1) Drug : Eligard® (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form Strength : 1) 45 Milligram
Form of Admin : 1) Injection
Lot Number : 1) Unknown
Daily Dose : (45 milligram(s), 1 in 6 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) Precocious puberty [10058084 - Precocious puberty]
Therapy Dates : 1) From : 31/Oct/2022 To :10/Jan/2025
Action(s) Taken With Drug : Unknown

Causality

1) Growth was a little advanced (Growth accelerated - 10018746, Growth accelerated - 10018746)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) Completion of treatment (Therapy cessation - 10065154, Therapy cessation - 10065154)
Causality as per reporter : Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Growth was a little advanced
CORE UnLabeled
2) Completion of treatment
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
Indications : 1) Precocious puberty [10058084 - Precocious puberty]
Action(s) Taken With Drug : Not applicable

Causality

1) Growth was a little advanced (Growth accelerated - 10018746, Growth accelerated - 10018746)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable

Continuation Sheet for CIOMS report

ReChallenge : Not Applicable

2) Completion of treatment (Therapy cessation - 10065154, Therapy cessation - 10065154)

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

Labeling :

1) Growth was a little advanced
CORE
2) Completion of treatment
CORE

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

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

Drug 2 :Eligard® Unspecified Device

1) UNK