

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last) UNKNOWN	1a. COUNTRY CHINA	2. DATE OF BIRTH			2a. AGE 1 Months	3. SEX Female	3a. WEIGHT 3.42 kg	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION ☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING ☐ CONGENITAL ANOMALY ☒ OTHER: IMPORTANT
		Day 26	Month JUN	Year 2025				Day 04	Month JUL	Year 2025	
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) Other Serious Criteria: Medically Significant, IMPORTANT MEDICAL EVENT PLATELETS DECREASED [Platelet count decreased] Case Description: Case reference number 2025CHF05807 is a report sent by other health professional and received through regulatory authority (regulatory authority number: 3301081750859202500126) via Chinese affiliate (local country number: CC202508017) which refers to a female patient aged 1 month (Han nationality). (Continued on Additional Information Page)											

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name) #1) PEYONA (CAFFEINE CITRATE) Solution for infusion and oral solution, 20 milligram per millilitre {Lot # 25815}		20. DID REACTION ABATE AFTER STOPPING DRUG? ☒ YES ☐ NO ☐ NA
15. DAILY DOSE(S) #1) 12 milligram, QD	16. ROUTE(S) OF ADMINISTRATION #1) Intravenous use	
17. INDICATION(S) FOR USE #1) APNOEA (Infantile apnoea)		21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA
18. THERAPY DATES(from/to) #1) 01-JUL-2025 / 05-JUL-2025	19. THERAPY DURATION #1) 4 days	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction) #1) Sodium chloride (Sodium chloride) Injection ; 01-JUL-2025 / 05-JUL-2025		
23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) From/To Dates Type of History / Notes Description Unknown		

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER Chiesi Farmaceutici SpA via Palermo, 26/A Parma, 43122 ITALY		26. REMARKS Medically Confirmed: Yes World Wide #: CN-CHIESI-2025CHF05807
	24b. MFR CONTROL NO. 2025CHF05807	25b. NAME AND ADDRESS OF REPORTER --- CHINA
24c. DATE RECEIVED BY MANUFACTURER 15-AUG-2025	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☒ OTHER: Regulatory Authority	
DATE OF THIS REPORT 22-AUG-2025	25a. REPORT TYPE ☒ INITIAL ☐ FOLLOWUP:	

22-Aug-2025 12:29

ADDITIONAL INFORMATION**7+13. DESCRIBE REACTION(S) continued**

Past medical/drug history have not been provided. The patient previous adverse drug reaction and family adverse drug reaction history were unknown.

On 01-Jul-2025 before medication, the patient's platelet count was at 204 billion per liter.

On 01-Jul-2025, the patient was administered Peyona [caffeine citrate] (solution for infusion and oral solution, 20mg/ml, intravenous, batch/lot no: 25815) at 12 mg daily for apnoea neonatal.

The patient was also under treatment with sodium chloride (injection) at 3 ml for solvent (medication dilution) (01-Jul-2025 to 05-Jul-2025).

On 04-Jul-2025, the patient experienced a significant medical event of platelet decreased. Relevant drugs were investigated and considered to be an adverse reaction of caffeine citrate injection.

On 04-Jul-2025, the patient's platelet count was at 27 billion per liter.

Suspected drug was withdrawn on 05-Jul-2025. After discontinuation, the platelet counts gradually increased.

On 09-Jul-2025, the platelet count was at 153 billion per liter, and on the same day the patient recovered from the event.

The reporter considered the event as possible related to Peyona.

No further information is expected as the case was received from regulatory authority.

Case comments:

This 1 month-old female neonate experienced platelets decreased while being treated with Peyona [caffeine citrate] (solution for infusion and oral solution, 20 mg/ml, intravenous use, batch/lot no: 25815) at 12 mg daily for apnoea neonatal.

The event platelets decreased was assessed as serious (seriousness criterion: medically significant).

The platelets decreased is not a listed adverse reaction for Peyona according to the reference safety information.

The adverse reaction of platelets decreased is unexpected as per Canadian Product Monograph.

It was reported that, on 04-Jul-2025, the patient's platelet count was at $27 \times 10^9/L$. Relevant drugs were investigated and considered to be an adverse reaction of Caffeine Citrate injection. Caffeine Citrate injection was immediately stopped on 05-Jul-2025. After discontinuation, the platelet count gradually increased.

With respect to platelets decreased, in the absence of relevant confounders, considering the drug to event temporal relationship and recovery of event after withdrawal of suspect drug, the causal role of suspect drug seems certain.

The company has assessed causal relationship between Peyona and platelets decreased as certain in accordance with the WHO-UMC causality assessment method.

The single individual case report does not modify the benefit / risk balance of this product. Therefore, no changes in the label or other measures are recommended at this point. However, the company will continue to monitor all respective reports received and based on cumulative experience, will re-evaluate the available evidence on an ongoing basis.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-JUL-2025	Platelet count	204 billion per litre	
2	04-JUL-2025	Platelet count	27 billion per litre	
3	09-JUL-2025	Platelet count	153 billion per litre	