SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	UNITED STATES	06	MAY	2025	1 Days	Male	Unk	07	MAY	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
CUROSURF OCCLUDED ET TUBE FOLLOWING DOSE ADMINISTRATION [Endotracheal intubation complication]
CUROSURF OCCLUDED ET TUBE FOLLOWING DOSE ADMINISTRATION [Product complaint]

Case Description: Case reference number 2025CHF03235 is a spontaneous case report sent by an other health professional via sales representative (hospital sales specialist) and received through US affiliate (local country

(Continued on Additional Information Page)

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

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) CUROSURF (PORACTANT ALFA) Endotracheopulmonary instillation, suspension, 80 milligram per millilitre

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 8.8 milliliter	#1) Unknown

17. INDICATION(S) FOR USE
#1) RESPIRATORY DISTRESS (Respiratory distress)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 06-MAY-2025 12:10:00 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

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 #: US-CHIESI-2025CHF03235

24b. MFR CONTROL NO.
2025CHF03235

25b. NAME AND ADDRESS OF REPORTER

UNITED STATES

24c. DATE RECEIVED BY MANUFACTURER
24-JUN-2025

24d. REPORT SOURCE
☐ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☒ OTHER: Spontaneous

DATE OF THIS REPORT
01-JUL-2025

25a. REPORT TYPE
☐ INITIAL ☒ FOLLOWUP: 1

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

number: CHIEMC-10103) which refers to a male patient of aged 1 day.

Concomitant medications and past medical/drug history have not been provided.

On 06-May-2025 at 12:10, the patient was administered Curosurf [poractant alfa] (endotracheopulmonary instillation, suspension, 80 mg/ml) at 8.8 ml for respiratory distress.

It was reported that the first dose had been given with no issues. Subsequently, a second dose was administered. This second dose was given in two halves. During the administration of the last half of the second dose on 07-May-2025 at 09:50, an occlusion was noticed in the endotracheal (ET) tube. As a result of this occlusion, the patient was extubated. To resolve the issue, the patient was then re-intubated (endotracheal tube obstruction) (seriousness: IME (important medical event) and pharmaceutical product complaint.

The event of endotracheal tube obstruction was considered as serious as it was included in the EMA IME list.

On 07-May-2025 at 09:55, the patient recovered from the event of endotracheal tube obstruction.

At the time of this report, the patient was not recovered yet from the event of pharmaceutical product complaint.

The reporter considered the event of endotracheal tube obstruction certainly related and did not assess the causal relationship between the event of pharmaceutical product complaint and Curosurf.

Further information is expected.

Update no.1 (24-Jun-2025)

This is significant follow up.

The investigation result of the returned sample, batch number N/A, linked to quality complaint (Trackwise number 311048) showed that the sample was not faulty, and the complaint was not justified.

The reason for complaint was the "Curosurf occluded ET tube following dose administration. The patient was extubated and reintubated to resolve issue. First dose given with no issues. 2nd dose given 1/2 at a time. Last half of dose was when occlusion was noticed.

Investigation included the reason of the complaint was “Curosurf occluded ET tube following dose administration”. No additional information were received after complaint’s notification on 09-May-2025. Without the sample and without the batch number it was not possible for the company to perform a complete investigation based on the reason of the complaint. Even if, according to the SOP the complaint could be closed as “not investigable”, considering the use of the product and its criticality being a lifesaver, we proceed with an overall evaluation in terms of quality aspect and complaint recurrence and incidence. The Product Quality Review (PQR) related to 2022-2023-2024 for US and ROW market data were verified as following: there were no critical or recurring non-conformities. No major change on the drug product manufacturing process, the good capability of the production process and the suitability of the applied control limits. From an analytical viewpoint, the quality of the product over the period considered proved to be constant and no anomalous trends were observed. The stability studies data were compliant with the shelf-life specifications, and the data obtained are aligned with the historical data of the product. All the release tests considered show that the quality of the product was comparable to the one shown along the previous years. An evaluation on the data analysis for relative density was performed as an additional investigation. The recorded data were verified from January 2022 to May 2025 on each Curosurf batches released by the company and all data were confirmed to be compliant to product specification without any out of trend data.

Complaints Evaluation: An evaluation of complaints (USA and ROW) of Curosurf product in the period 2022-2023-2024-2025 was carried out. 17 out of 71 complaints for Curosurf product were received for thick or unexpected consistence and were evaluated below. 16 complaints were received from USA: 10 complaints (9 in 2022 and 1 in 2023) without batch number (Reference numbers TW 153612, 167765, 172227, 172230, 172252, 174485, 174486, 174492, 185402, 185409, in trackwise system) 6 complaints (4 in 2022 and 2 in 2023) regarding batches 1159795, 1160333 of Curosurf 1,5ml and 1141015, 1142773, 1148042, 1141015 of CUROSURF 3ml US (Reference numbers TW 153609, 165127, 170219, 170456, 202352, 204149 in Trackwise system). 1 complaint was received from ROW: 1 complaint from Germany in January 2024 regarding Curosurf 1.5 ml batch 1165818 (Reference TW 236838 Trackwise system). All 17 complaints were closed and all were judged as not justified. The investigation performed on the sample, when available, or on retained sample did not detect any non-conformities in the manufacturing processes and confirmed that the product was compliant to specifications. Considering the number of complaints received and the quantity of vials sold during the period 2022-2023-2024-2025, the ppm calculated was 9: the events notified for Curosurf product were considered very low, the issues reported were non-systematic and not attributable to a qualitative defect of the batches involved. Conclusions: the evaluation of complaints (USA and ROW) received for thick or unexpected consistence of Curosurf product in the period 2022-2023-2024-2025 did not highlight any critical situation. Without the sample and without the batch number it was not possible for the company to carry out other investigations. kindly suggested to closely follow the leaflet instructions.

On an unspecified date, the patient recovered from the event of pharmaceutical product complaint.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

No further information is expected as the case has sufficient information for assessment.

Case comments:
This 1 day old male neonate experienced “Curosurf occluded ET tube following dose administration” (endotracheal tube obstruction) (pharmaceutical product complaint) during administration of Curosurf [poractant alfa] (endotracheopulmonary instillation, suspension, 80 mg/ml) at a dose of 8.8 ml for respiratory distress.
The event “Curosurf occluded ET tube following dose administration” was assessed as serious (seriousness criterion: important medical event).
The event of endotracheal tube obstruction was considered as serious as it is included in the EMA IME list.
The event “Curosurf occluded ET tube following dose administration” was considered as non-serious by convention.
The endotracheal tube obstruction is a listed adverse reaction for Curosurf according to the reference safety information.
The pharmaceutical product complaint was considered as unlisted by convention.
The adverse reaction of endotracheal tube obstruction is expected as per US Prescribing Information.
The pharmaceutical product complaint was considered as unexpected by convention.
The adverse reaction of endotracheal tube obstruction is expected as per Canadian Product Monograph.
The pharmaceutical product complaint was considered as unexpected by convention.
With reference to endotracheal tube obstruction, although information pertaining to concomitant medications and concurrent conditions are not available, considering drug to event temporal relationship and known safety profile, the causal role of suspect drug cannot be denied.
The company has assessed the causal relationship between Curosurf and endotracheal tube obstruction as possible in accordance with the WHO-UMC causality assessment method.
With respect to pharmaceutical product complaint, investigational results refute product quality issue.
The company has assessed causal relationship between Curosurf and pharmaceutical product complaint as unlikely as per convention.
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.