CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	TURKEY		Unk		Unk	Female	3.48 kg	16	JAN	2025

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

DEATH NOS [Death]
THE PATIENT WAS PRESCRIBED THE DRUG FOR PRIMARY OR SECONDARY SURFACTANT DEFICIENCY [Off label use]
THE PATIENT ADMINISTERED 3 VIALS OF CUROSURF 240 (720 MG) AT ONCE ON 16-JAN-2025 [Off label use]
THE PATIENT ADMINISTERED 3 VIALS OF CUROSURF 240 (720 MG) AT ONCE ON 16-JAN-2025 [Prescribed overdose]
THE PATIENT ADMINISTERED 3 VIALS OF CUROSURF 240 (720 MG) AT ONCE ON 19-JAN-2025 [Off label use]
THE PATIENT ADMINISTERED 3 VIALS OF CUROSURF 240 (720

(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

II. SUSPECT DRUG(S) INFORMATION

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

15. DAILY DOSE(S)
#1) 720 milligram, (1X)

16. ROUTE(S) OF ADMINISTRATION
#1) Intratracheal

17. INDICATION(S) FOR USE
#1) PRIMARY OR SECONDARY SURFAC
(Continued on Additional Information Page)

18. THERAPY DATES(from/to)
#1) 16-JAN-2025 / 16-JAN-2025

19. THERAPY DURATION
#1) Unknown

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

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

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) Meropenem (Meropenem) 78 milligram; Unknown
#2) Vancomycin (Vancomycin hydrochloride) 40 milligram; Unknown
#3) Klamer (Clarithromycin) Suspension, 40 milligram; Unknown
#4) Sildenafil (Sildenafil citrate) Suspension, 4 milligram; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Historical Condition	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Chiesi Farmaceutici SpA
via Palermo, 26/A
Parma, 43122 ITALY

26. REMARKS
Medically Confirmed: No
World Wide #: TR-CHIESI-2025CHF01341

24b. MFR CONTROL NO.
2025CHF01341

25b. NAME AND ADDRESS OF REPORTER

TURKEY

24c. DATE RECEIVED BY MANUFACTURER
20-MAR-2025

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

DATE OF THIS REPORT
03-JUN-2025

25a. REPORT TYPE
☐ INITIAL ☒ FOLLOWUP: 2

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

MG) AT ONCE ON 19-JAN-2025 [Prescribed overdose]
THE PATIENT ADMINISTERED 3 VIALS OF CUROSURF 240 (720 MG) AT THE INTERVAL OF 3 DAYS [Off label use]

Case Description: Case reference number 2025CHF01341 is a spontaneous case report sent by consumer and received through Turkish affiliate (local country number: 2025TR00001-Curosurf) which refers to a female patient aged 39 weeks.

Past drug history has not been provided.

The patient had a medical history of primary or secondary surfactant deficiency (surfactant deficiency syndrome neonatal).

On 16-Jan-2025, the patient was given Curosurf [poractant alfa] (endotracheopulmonary instillation, suspension, 80 mg/ml) at a dose of 3 vials of 240 mg (total dose of 720 mg) once, then on 19-Jan-2025, again 3 vials of 240 mg (total dose of 720 mg) once for secondary surfactant deficiency, use in patient aged 39-weeks (surfactant deficiency syndrome neonatal).

The patient was also under the treatment with Meropenem (78 mg) at a dose of 78 mg twice daily, IV daily, Vancomycin [vancomycin hydrochloride] (40 mg) at a dose of 40 mg twice daily, Klamer [clarithromycin] (oral suspension, 40 mg), at a dose of 40 mg twice daily, oral, Sildenafil [sildenafil citrate] (oral suspension, 4 mg) at a dose of 4 mg thrice daily, oral.

As per local RSI, Curosurf is indication for prophylactic use and treatment of premature infants with or at risk for respiratory distress syndrome. However, as the patient was prescribed Curosurf for primary or secondary surfactant deficiency, this constituted an event of off label use.

Also, as per local RSI, the recommended starting dose is 100-200 mg/kg (1.25-2.5 ml/kg) , administered in a single dose as soon as possible after diagnosing RDS. Additional doses of 100 mg/kg (1.25 ml/kg), each at about 12-hourly intervals, may also be administered if RDS is considered to be cause of persisting or deteriorating respiratory status of the infants (maximum total dose of 300-400 mg/kg). Since the patient was administered 3 vials of Curosurf 240 (total dose of 720 mg) once on 16-Jan-2025 and once on 19-Jan-2025 after the interval of 3 days, which is more than maximum recommended dose, these constituted the events of off label dosing, prescribed overdose, off label dosing, prescribed overdose and off label dosing.

On 16-Jan-2025, patient recovered from the events of off label dosing, prescribed overdose.

On 19-Jan-2025, patient recovered from the events of off label dosing, prescribed overdose and off label use.

On 23-Jan-2025, the patient was referred to another hospital for neonatal intensive care.

On 24-Feb-2025, the reporter was informed that the patient died in the hospital to which he was referred. The date of death was unknown.

The reporter did not assess the causal relationship between the events and Curosurf.

No further information is expected as sufficient information available.

Update no. 01 (20-Mar-2025)

This is a significant follow up.

It was confirmed that age reported 39 weeks was gestational age.

No further information is expected as sufficient information available.

Amendment no. 01 (20-Mar-2025)

This is non-significant amendment to add the event.

On an unspecified date the patient died. It was unknown if autopsy was performed or not.

The reporter considered the event of death NOS as not related to Curosurf.

Case comments:
This female neonate patient experienced death NOS, “the patient was prescribed the drug for primary or secondary surfactant deficiency” (off label use), “the patient administered 3 vials of Curosurf 240 (720 mg) at once on 16-Jan-2025” (off label dosing) (prescribed overdose), “the patient administered 3 vials of Curosurf 240 (720 mg) at the interval of 3 days” (off label dosing) and “the patient administered 3 vials of Curosurf 240 (720 mg) at once on 19-Jan-2025” (off label dosing) (prescribed overdose) while being treated with Curosurf [poractant alfa] (endotracheopulmonary instillation, suspension, 80 mg/ml, intratracheal) at a dose of 3 vials of 240 mg (total dose of 720 mg) once, then on 19-Jan-2025, again 3 vials of 240 mg (total dose of 720 mg) once for primary or secondary surfactant deficiency (surfactant deficiency syndrome neonatal).

Mfr. Control Number: 2025CHF01341

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The event death NOS was assessed as serious (seriousness criterion: death).
The events “the patient was prescribed the drug for primary or secondary surfactant deficiency”, “the patient administered 3 vials of Curosurf 240 (720 mg) at once on 16-Jan-2025”, “the patient administered 3 vials of Curosurf 240 (720 mg) at the interval of 3 days” and “the patient administered 3 vials of Curosurf 240 (720 mg) at once on 19-Jan-2025” were considered as non-serious by convention.
The death NOS is not a listed adverse reaction for Curosurf according to the reference safety information. The prescribed overdose and prescribed overdose were considered as unlisted by convention. According to the local RSI, the off label dosing, off label use, off label dosing and off label dosing were considered as unlisted.
The adverse reaction of death NOS is unexpected as per US Prescribing Information. The prescribed overdose and prescribed overdose were considered as unexpected by convention. The off label dosing, off label use, off label dosing and off label dosing were considered as unexpected as per US Prescribing Information.
The adverse reaction of death NOS is unexpected as per Canadian Product Monograph. The prescribed overdose and prescribed overdose were considered as unexpected by convention. The off label dosing, off label use, off label dosing and off label dosing were considered as unexpected as per Canadian Product Monograph.
With respect to death NOS, underlying condition of primary or secondary surfactant deficiency could provide a plausible explanation and there seems no role of suspect drug in the causation of event.
The company has assessed causal relationship between Curosurf and death NOS as not related in accordance with the WHO-UMC causality assessment method.
As per local RSI, Curosurf is indication for prophylactic use and treatment of premature infants with or at risk for respiratory distress syndrome. However, as the patient was prescribed Curosurf for primary or secondary surfactant deficiency, this constituted an event of off label use.
Also, as per local RSI, the recommended starting dose is 100-200 mg/kg (1.25-2.5 ml/kg) , administered in a single dose as soon as possible after diagnosing RDS. Additional doses of 100 mg/kg (1.25 ml/kg), each at about 12-hourly intervals, may also be administered if RDS is considered to be cause of persisting or deteriorating respiratory status of the infants (maximum total dose of 300-400 mg/kg). Since the patient was administered 3 vials of Curosurf 240 (total dose of 720 mg) once on 16-Jan-2025 and once on 19-Jan-2025 after the interval of 3 days, which is more than maximum recommended dose, these constituted the events of off label dosing, prescribed overdose, off label dosing, prescribed overdose and off label dosing.
Causality was assessed as not applicable for off label use, prescribed overdose, off label dosing, prescribed overdose, off label dosing and off label dosing as these were not events per se.
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.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) CUROSURF (PORACTANT ALFA) Endotracheopulmonary instillation, suspension, 80 milligram per millilitre; Regimen #1	720 milligram, (1X); Intratracheal	PRIMARY OR SECONDARY SURFACTANT DEFICIENCY (Neonatal respiratory distress syndrome) OFF LABEL USE (Off label use)	16-JAN-2025 / 16-JAN-2025; Unknown
#1) CUROSURF (PORACTANT ALFA) Endotracheopulmonary instillation, suspension, 80 milligram per millilitre; Regimen #2	720 milligram, (1X); Intratracheal	PRIMARY OR SECONDARY SURFACTANT DEFICIENCY (Neonatal respiratory distress syndrome) OFF LABEL USE (Off label use)	19-JAN-2025 / 19-JAN-2025; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Historical Condition	Surfactant deficiency syndrome neonatal (Neonatal respiratory distress syndrome);