

Data Sheet

CUROSURF®

Poractant alfa (Phospholipid fraction of porcine lung) 80 mg/ml

Presentation

Sterile suspension in single-dose vials for intratracheal or intrabronchial administration.

One 1.5ml clear, colourless vial closed with a chlorobutyl rubber stopper contains phospholipid fraction from porcine lung, 120 mg (80 mg/ml). The stopper is held in place by an aluminium ring and covered with a plastic cap.

One 3 ml clear, colourless vial closed with a chlorobutyl rubber stopper contains phospholipid fraction from porcine lung, 240 mg (80 mg/ml). The stopper is held in place by an aluminium ring and covered with a plastic cap.

Uses

Actions

CUROSURF® is a natural surfactant, prepared from porcine lungs, containing almost exclusively phospholipids, in particular phosphatidylcholine (about 70% of the total phospholipid content) and about 1% of specific low molecular weight hydrophobic proteins SP-B and SP-C.

Lung surfactant is a mixture of substances, mainly phospholipids and specific proteins, lining the internal surface of alveoli. Their main function is to lower pulmonary surface tension. This surface tension lowering activity is essential to stabilise alveoli, and to avoid collapse at the end of expiration, so that adequate gas exchange is maintained throughout the ventilatory cycle.

Deficiency of lung surfactant, from whatever cause leads to severe respiratory failure, which in preterm babies is known as respiratory distress syndrome (RDS) or hyaline membrane disease (HMD). RDS is a major cause of acute mortality and acute morbidity in the preterm baby and may also be responsible for long-term respiratory and neurologic sequelae.

CUROSURF® was developed to replace this deficiency of endogenous pulmonary surfactant by intratracheal administration of exogenous surfactant.

The surfactant properties of CUROSURF® favour its uniform distribution in the lungs and spreading at the air-liquid interfaces in the alveoli.

The therapeutic effects of CUROSURF® have been documented in babies with RDS and preterm babies at risk for RDS. Preterm newborn infants treated with a single dose of CUROSURF® (1.25-2.5 ml/kg equal to 100-200 mg/kg of phospholipids) showed a rapid and dramatic improvement of oxygenation with reduction of the inhaled oxygen concentration (FiO₂) and increase of PaO₂, and of PaO₂/ FiO₂ and a/APO₂ ratios. Mortality rate and incidence of major pulmonary complications were shown to be reduced.

The administration of a second or third dose of 100 mg/kg seems to further reduce the incidence of pneumothorax and mortality.

Pharmacokinetics

CUROSURF® remains mainly in the lungs following intratracheal administration. A half-life of 67 hours of ¹⁴C-labelled dipalmitoyl-phosphatidylcholine has been measured in newborn rabbits.

48 hours after administration, only traces of surfactant lipids could be found in serum and organs other than lungs.

Indications

Treatment of Respiratory Distress Syndrome (RDS) in pre-term babies.

Prophylactic use in premature infants at risk for RDS.

Dosage and Administration

Rescue treatment: The recommended dose is a single dose of 100-200 mg/kg (1.25-2.5 ml/kg) of body weight. It is possible to administer additional doses of 100 mg/kg, each one at about 12-hourly intervals, in infants still requiring assisted ventilation and supplementary oxygen (maximum total dose: 300-400 mg/kg). It is recommended to start treatment as soon as possible after diagnosing RDS.

Prophylaxis: a single dose of 100-200 mg/kg should be administered as soon as possible (within 15 minutes) after birth. Further doses of 100 mg/kg can be given 6-12 hours after the first dose, and then at 12 hourly intervals in case of occurrence of RDS requiring mechanical ventilation (max. total dose: 300-400 mg/kg).

Method of Administration: CUROSURF® is available in ready-to-use vials that should be stored in a refrigerator at +2 to +8°C. The vial should be warmed to 37°C before use, and gently turned upside down, without shaking, in order to obtain a homogeneous suspension.

The suspension should be withdrawn from the vial by using a sterile needle and syringe, and directly administered, via the intratracheal tube, as a single

dose into the lower part of the trachea, or as two halved doses into the main right and left bronchial tubes, respectively.

Perform approximately one minute of manual ventilation with the same percentage of oxygen as before administration, in order to favour a uniform distribution.

Reconnect the baby to the ventilator, whose parameters must be suitably adjusted to the clinical response and to changes in blood gases.

Administer any further required doses in the same manner.

Babies not requiring assisted ventilation can be disconnected from the ventilator after CUROSURF® administration.

It is recommended to frequently control blood gases, as, after administration, an immediate increase of PaO₂ or oxygen saturation is generally observed (See Warnings and Precautions).

It is however advisable to continuously monitor transcutaneous PO₂ or oxygen saturation to avoid hyperoxia.

Contraindications

No specific contraindications are known yet.

Warnings and Precautions

CUROSURF® should only be administered in hospital, by those trained and experienced in the care and resuscitation of preterm infants, where suitable equipment for ventilation and monitoring of babies with RDS is available.

Efficacy has not been shown following prolonged rupture of the membranes (longer than 3 weeks) or clearly shown in infants with meconium aspiration or group B streptococcal infection.

The baby's general conditions should be stabilised. Correction of acidosis, hypotension, anaemia, hypoglycaemia and hypothermia is also recommended.

CUROSURF® has a very rapid onset of action. It is, therefore, necessary to frequently monitor infants receiving CUROSURF® by arterial or transcutaneous measurement of systemic oxygen and carbon dioxide.

Transient episodes of bradycardia, hypotension and decreased oxygen saturation have been reported after administration of surfactants. If these occur, stop administration of CUROSURF® and initiate appropriate measures

to alleviate the condition. After the condition is stabilised, resume administration.

Surfactant administration can be expected to reduce the severity of RDS or the risk of its reoccurrence, but cannot be expected to completely eliminate mortality and morbidity associated with preterm birth, as preterm babies may be exposed to other complications due to their immaturity.

Acute toxicity studies in different animal species administered CUROSURF[®] by intraperitoneal and intratracheal routes did not elicit either signs of lung or systemic toxicity, or mortality. Subacute intratracheal toxicity studies (14 days) in dogs, rabbits and rats showed neither clinical effects nor haematological changes, nor macroscopic variations related to the treatment. Moreover, CUROSURF[®] did not reveal any evidence of direct toxicity in the rat by intraperitoneal route (4 weeks).

CUROSURF[®] given by parenteral route in guinea pigs neither elicits active anaphylactic reactions, nor stimulates the production of antibodies detectable by passive cutaneous anaphylactic reaction. No anaphylactic reaction was observed by intratracheal route. Furthermore, there is no evidence of dermal sensitising potential (Magnusson and Kligman test).

CUROSURF[®] did not show any evidence of mutagenic or clastogenic activity.

Adverse Effects

Transient adverse effects seen with the administration of surfactants include bradycardia, hypotension, endotracheal tube blockage, and oxygen desaturation.

Pulmonary haemorrhage, the incidence of which increases with immaturity of the infant, is a rare and sometimes fatal complication of preterm delivery. No evidence exists of any risk of this event following the administration of CUROSURF[®].

Interactions

Not known.

Overdosage

There have been no reports of overdosage following the administration of CUROSURF[®]. However, in the unlikely event of accidental overdose, and only if there are clear clinical effects on the infant's respiration, ventilation or oxygenation, as much of the suspension as possible should be aspirated and

the baby should be managed with supportive treatment, paying particular attention to fluid and electrolyte balance.

Pharmaceutical Precautions

Shelf life is 18 months. This shelf-life refers to the unopened and correctly stored product.

The product must be stored at +2 to +8°C, protected from light. Unused vials may be warmed to room temperature for up to 24 hours before use, but warmed vials should not be returned to the refrigerator. After opening, discard the unused portion of the medicine.

Medicine Classification

Prescription Medicine

Package Quantities

One 1.5 ml vial contains:

Active ingredient: phospholipid fraction from porcine lung 120 mg.

One 3 ml vial contains:

Active ingredient: phospholipid fraction from porcine lung 240 mg.

Further Information

The physiological and therapeutic effects of CUROSURF® in surfactant deficiency have been extensively documented in various animal models.

In immature rabbit foetuses obtained by hysterectomy and immediately sacrificed the administration of CUROSURF® caused a marked improvement in lung expansion. In premature newborn rabbits ventilated with 100% oxygen there was a dramatic improvement of tidal volume and lung-thorax compliance, compared to the control animals, after administration of CUROSURF® via a tracheal cannula. Also in premature newborn rabbits, treatment with CUROSURF® (maintaining a standardised tidal volume of about 10 ml/kg) increased the compliance of the lung-thorax system to a level similar to that of mature newborn animals.

Excipients:

Sterile sodium chloride for injection containing sodium chloride and water.

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