PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

Survanta 25 mg/ml sterile dispersion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Total phospholipids (beractant) 25 mg

(including disaturated phosphatidylcholines 11,0 – 15,5 mg)

Triglycerides 0,5 to 1,75 mg

Free Fatty Acids 1,4 to 3,5 mg

Protein 0,1 to 0,4 mg

Excipient with known effect: 3,54 mg/ml Sodium

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Sterile dispersion.

Off-white to light brown opaque liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Survanta is indicated in the treatment and prevention of neonatal respiratory distress syndrome (RDS).

4.2 Posology and method of administration

Posology

Paediatric population

The recommended dose of Survanta is 100 mg phospholipid/kg body weight in a volume not exceeding 4 ml/kg.

Treatment should be administered early in the course of Respiratory Distress Syndrome, i.e. preferably babies less than 8 hours of age.

For treatment and prophylaxis of RDS in high-risk infants, up to four doses of Survanta may be administered within 48 hours. The first dose is given at 15 minutes postpartum, with up to three additional doses at intervals of at least six hours.

Method of administration

Before administration, Survanta should be warmed by standing at room temperature for about 20 minutes or warmed in the hand for 8 minutes. ARTIFICIAL METHODS OF WARMING SHOULD NOT BE USED.

If settling has occurred during storage, redisperse by swirling the vial gently. Slowly withdraw the entire contents of the vial into a plastic syringe through a large-gauge needle, i.e. 20 gauge or larger. DO NOT FILTER SURVANTA.

Survanta is administered intratracheally. It can be instilled 1) through a 5 French end-hole catheter inserted into the infant's endotracheal tube by briefly disconnecting the endotracheal tube from the ventilator or 2) by inserting the catheter through a neonatal suction valve without disconnecting the endotracheal tube from the ventilator.

If the medicine is instilled through an end-hole catheter, the length of the catheter should be shortened so that the tip of the catheter protrudes just beyond the end of the endotracheal tube above the infant's carina. Survanta should not be instilled into a mainstream bronchus.

To ensure homogenous distribution of Survanta throughout the lungs, each dose is divided into fractional doses. Each dose can be administered in two half-doses or in four quarter-doses. Each fractional dose is administered with the infant in a different position. To administer Survanta in two half-doses, the recommended positions are:

- Head and body turned approximately 45 deg. to the right.
- Head and body turned approximately 45 deg. to the left.

To administer Survanta in four quarter-doses, the recommended positions are:

- Head and body inclined slightly downwards, head and body turned to the right.
- Head and body inclined slightly downwards, head and body turned to the left.

- Head and body inclined slightly upwards, head and body turned to the right.

- Head and body inclined slightly upwards, head and body turned to the left.

It is recommended that Survanta be administered in two half-doses through a neonatal suction valve.

AFTER COMPLETION OF THE DOSING PROCEDURE, RESUME USUAL VENTILATOR MANAGEMENT AND CLINICAL CARE.

4.3 Contraindications

No specific contraindications for Survanta have been defined by the clinical studies.

4.4 Special warnings and precautions for use

Survanta should only be administered with adequate facilities for ventilation and monitoring of babies with RDS.

Marked improvements in oxygenation may occur within minutes of the administration of Survanta. Therefore, frequent and careful monitoring of systemic oxygenation is essential to avoid hyperoxia. Following Survanta administration, monitoring of the arterial blood gases, the fraction of inspired oxygen and ventilatory change is required to ensure appropriate adjustments.

During the dosing procedure, transient episodes of bradycardia and/or oxygen desaturation have been reported. If these occur, dosing should be stopped and appropriate measures to

alleviate the condition should be initiated. After stabilisation, the dosing procedure should be resumed.

4.5 Interaction with other medicines and other forms of interaction

Interactions between Survanta and other medicines commonly used concomitantly in neonatal intensive care, e.g. catecholamines, indomethacin, tolazoline, pancuronium, phenobarbital, opiates, antibiotics and parenteral nutrients, have not been observed.

Additionally, medicines such as tocolytics and corticosteroids given prenatally to mothers did not interfere with the use of Survanta in the neonate.

4.6 Fertility, pregnancy and lactation

Not applicable.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Paediatric population

a. Summary of the safety profile

Mechanically Ventilated Infants

Intracranial haemorrhage has been observed in patients who received either beractant or placebo. The incidence of intracranial haemorrhage in all patients is similar to that reported

in the literature in this patient population. Pulmonary haemorrhage has also been reported. Blockage of the endotracheal tube by mucous secretions has been reported. No other serious adverse reactions have been reported.

b. **Tabulated summary of adverse reactions**

The following adverse reactions were identified in patients treated with Survanta. The adverse reactions are listed below by body system organ class and frequency. Frequencies are defined as follows: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000) or not known (cannot be estimated from the available data).

These are presented in the following table:

System Organ Class	**Frequency**	**Adverse Reactions**
Vascular disorders	Very common	Intracranial haemorrhage
Respiratory	Common	Pulmonary haemorrhage
Surgical and Medical Procedures	Uncommon	Blockage of endotracheal tube by mucous secretions

No antibody production to Survanta proteins has been observed.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Paediatric population

If an excessively large dose of Survanta is given, observe the infant for signs of acute airway obstruction. Treatment should be symptomatic and supportive. Rales and moist breath sounds may occur transiently after Survanta is given and do not indicate overdosage. Endotracheal suctioning or other remedial action is not required unless clear-cut signs of airway obstruction are present.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 10.2.2 Other (Pulmonary surfactant)

The mode of action of Survanta is biophysical rather than biochemical, i.e. it reduces surface tension and concomitantly increases lung compliance.

Intratracheally administered Survanta distributes rapidly to the alveolar surfaces and stabilises the alveoli against collapse during respiration, thereby increasing alveolar ventilation.

Mechanically ventilated infants

In clinical studies of premature infants with respiratory distress syndrome (RDS), a significant improvement of oxygenation was demonstrated after treatment with a single dose of Survanta.

These infants showed a decreased need for supplemental oxygen and an increase in the arterial/alveolar oxygen ratio (a/ApO_2). A significantly decreased need for respiratory support, as indicated by a lower mean airway pressure, was also observed. In most cases these effects were maintained for at least 72 hours after the administration of a single dose of Survanta.

5.2 Pharmacokinetic properties

In pre-clinical studies using radio-labelled phosphatidylcholine, the clearance rate of Survanta in the lung of three day old rabbits has been shown to be similar to that of natural calf and sheep surfactants (approximately 13 % within 24 hours). In addition, some re-uptake and secretion of Survanta was shown, implying its entry into a metabolically-active surfactant pool.

Since an exogenous preparation of Survanta is delivered directly to the lung, classical clinical pharmacokinetic parameters (blood levels, plasma half-life etc.) have not been studied.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dipalmitoyl Phosphatidylcholine

Palmitic acid

Tripalmitin

Sodium chloride

Water for injection

Sodium Hydroxide

Hydrochloric acid

6.2 Incompatibilities

None experienced to date, as product administration is unique.

6.3 Shelf life

18 months

Before administration, Survanta should be warmed by standing at room temperature for 20 minutes or warmed in the hand for 8 minutes. ARTIFICIAL WARMING METHODS SHOULD NOT BE USED.

Unused vials: unopened, unused vials of Survanta that have been warmed to room temperature may be returned to the refrigerator within 24 hours of warming and stored for future use. Survanta should not be warmed and re-refrigerated more than once.

6.4 Special precautions for storage

Store under refrigerated conditions (2 - 8 ºC) protected from light.

Do not freeze. Any inadvertently frozen product should be discarded. For storage conditions after product is removed from the refrigerator before opening, see section 6.3.

6.5 Nature and contents of container

Single glass vial containing 4 ml or 8 ml of liquid.

6.6 Special precaution for disposal and other handling

Each vial of Survanta is for single use only. Used vials with residual medicine should be discarded.

Survanta should be inspected visually for discolouration prior to administration. The colour of Survanta is off-white to light brown. Some settling may occur during storage. If this occurs, gently invert the vial several times (DO NOT SHAKE) to redisperse.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER(S)

Z/10.2.2/211

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

05 November 1991

10 DATE OF REVISION OF THE TEXT

09 November 2022