SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Survanta 25mg/ml suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains beractant equivalent to:

Phospholipids	25 mg/ml
(including disaturated phosphatidylcholines	11.0 - 15.5 mg/ml)
Triglycerides	0.5 - 1.75 mg/ml
Free Fatty Acids	1.4 - 3.5 mg/ml
Protein	0.1 - 1.0 mg/ml

Excipient with known effect: 3.54mg/ml Sodium

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Sterile suspension for intratracheal administration

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Survanta is indicated for treatment of Respiratory Distress Syndrome (RDS) (hyaline membrane disease) in new born premature infants with a birth weight of 700g or greater.

Survanta is also indicated for the prophylactic treatment of premature infants <32 weeks gestational age at risk of developing RDS who require intubation for stabilisation or with evidence of surfactant deficiency.

4.2 Posology and method of administration

Posology

Paediatric population

100 mg phosholipid/kg birth weight in a volume not exceeding 4ml/kg.

Treatment: The first dose of Survanta should be given as soon as possible after RDS is confirmed by radiographic or clinical findings. Depending on clinical course, this dose may be repeated within 48 hours at intervals of at least six hours for up to 4 doses.

Prophylaxis: The first dose of Survanta should be administered as soon as possible after birth, preferably within 15 minutes. Depending on clinical course, this dose may be repeated within 48 hours at intervals of at least six hours for up to 4 doses.

Method of Administration
Survanta should be administered via the endotracheopulmonary route.

The dosing procedure is facilitated if one person administers the dose while another person positions and monitors the infant.

Survanta should be warmed to room temperature before administration (see section 6.3).

Instillation in Mechanically Ventilated Infants

Before administering Survanta to infants on mechanical ventilation, suggested settings include respiratory frequency at 60/minute, inspiration time 0.5s, and F_i0_2 at 1.0. Inspiratory pressure needs no change at this point.

There are 2 alternative methods of administration for mechanically ventilated infants:

i. The dose is administered by disconnecting the endotracheal tube from the ventilator, inserting a small diameter catheter and administering the dose with the infant in a neutral position. The tip of the catheter should lie at the end of the endotracheal tube.

Alternatively:

ii. The dose can be administered by inserting a small diameter catheter through a suction port connector without disconnection from the ventilator with the infant in a neutral position. The tip of the catheter should lie at the end of the endotracheal tube.

After the dose is administered, the catheter is then withdrawn completely, and the ventilator is reconnected if necessary.

Instillation in Spontaneously Breathing Infants

Intubation Surfactant Extubation (INSURE)
Following intubation and insertion of the catheter as described above, place the infant in a neutral position and gently inject the dose as a single bolus over 1 to 3 minutes in the delivery room or later after admission to the neonatal unit. After instillation, use a bagging technique and proceed to extubation and CPAP as clinically indicated.

Less Invasive Surfactant Administration (LISA)
A small diameter catheter may be used to administer the dose without intubation. In such cases, place the catheter directly into the trachea of infants on CPAP with direct

visualization of the vocal cords by laryngoscopy and gently inject the dose as a single bolus over 1 to 3 minutes. After instillation, immediately remove the catheter. Ensure continuous spontaneous breathing and continue CPAP treatment during the entire procedure.

Dosage in Adults
Not applicable.

Dosage in Older People
Not applicable.

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 Interactions with other Medicinal Products and other forms of Interaction

No interaction studies have been performed.

4.6 Fertility, Pregnancy and lactation

No interaction studies have been performed.

4.7 Effects on ability to drive and use machines

Not relevant

4.8 Undesirable effects

Paediatric population

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.

INSURE and LISA Techniques
Safety results with the INSURE and LISA techniques were comparable to those of the control groups, although bradycardia and hypoxemia were reported more frequently in some cases with LISA.

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 medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme:

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

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 can transiently occur after Survanta is given, and do not indicate overdosage. Endotracheal suction or other remedial action is not required unless clear-cut signs of airway obstruction are present.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Lung Surfactant
ATC Code R07AA02

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 in 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 ($a/Ap0_2$). 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 the single dose of Survanta.

LISA Technique
The LISA method of administration was evaluated in two multicenter and seven single-center studies identified from the published scientific literature. A total of 745 infants were treated with Survanta via LISA with an additional 583 infants treated with Survanta via endotracheal tube as control groups. All infants were administered a dose of 100 mg/kg birth weight. Individual study mean gestational ages ranged from 25.3 weeks to 32 weeks with mean weights ranging from 610 g to 1865 g. Overall, infants treated with CPAP and LISA had a reduced need for mechanical ventilation, reduced duration of mechanical ventilation, and reduced oxygen requirement. In some of the studies, a reduced risk of development of bronchopulmonary dysplasia due to RDS was seen.

5.2 Pharmacokinetic properties

In preclinical studies using radiolabelled 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 pharmocokinetic parameters (blood levels, plasma half-life etc.) have not been studied.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Palmitic acid
Dipalmitoyl Phosphatidylcholine
Tripalmitin
Sodium Hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
Water for injection

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. Discard each vial if not used within 8 hours of warming to room temperature. Vials should not be returned to the refrigerator once warmed.

6.4 Special precautions for storage

Store under refrigerated conditions (2-8ºC) 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

21ml glass bottle with a 20mm rubber stopper and a 20mm aluminium seal finish containing 8ml of product.

Pack sizes: 1, 3 and 10

6.6 Special precautions for disposal and other handling

Each vial of Survanta is for single use only. Used vials with residual drug 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 MARKETING AUTHORISATION HOLDER

AbbVie Ltd.
Maidenhead
SL6 4UB
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 41042/0003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 3 February 1993
Date of last renewal: 21 October 2004

10 DATE OF REVISION OF THE TEXT

14/07/2020