AUSTRALIAN PRODUCT INFORMATION – SURVANTA®

(BERACTANT) INTRATRACHEAL SUSPENSION

1 NAME OF THE MEDICINE

Beractant.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Survanta® (beractant) is a sterile, non-pyrogenic pulmonary surfactant intended for intratracheal use only. It is a natural bovine lung extract containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins to which colfosceril palmitate (dipalmitoyl phosphatidylcholine), palmitic acid and tripalmitin are added to standardise the composition and to mimic the surface-tension lowering properties of natural lung surfactant. It is dispersed in 0.9% sodium chloride solution and heat-sterilised. Survanta contains no preservatives. It contains two, hydrophobic, low molecular weight, surfactant-associated proteins commonly known as SP-B and SP-C. It does not contain the hydrophilic, large molecular weight surfactant-associated protein known as SP-A.

Each mL of Survanta contains beractant equivalent to 25 mg of phospholipids (200 mg phospholipids / 8mL) suspended in 0.9% sodium chloride solution.

3 PHARMACEUTICAL FORM

Survanta (beractant) intratracheal suspension is an off-white to light brown liquid supplied in single-use glass vials.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Survanta is indicated for prevention and treatment ("rescue") of Respiratory Distress Syndrome (RDS) (hyaline membrane disease) in premature infants.

Prevention

In premature infants less than 1250 g birthweight, or with evidence of surfactant deficiency, give Survanta as soon as possible, preferably within 15 minutes of birth.

Rescue

To treat infants with RDS confirmed by X-ray and requiring mechanical ventilation, give Survanta as soon as possible, preferably by 8 hours of age.

NOTE: Results from clinical studies suggest that little benefit is likely to be gained from giving Survanta to infants who have completed a prenatal course of corticosteroids, unless they develop RDS within the first 6-8 hours of life.

The results of outborn compared to inborn infants were not analysed separately in the clinical trials.

Outborn infants were distributed equally between the treatment groups and were not considered likely to bias the estimation of treatment effect. Therefore, there does not appear to be any evidence to suggest that outborn infants respond less well to treatment with Survanta.

4.2 Dose and method of administration

For Intratracheal Administration Only

Survanta should be administered by or under the supervision of clinicians experienced in intubation, ventilator management and general care of premature infants.

Marked improvements in oxygenation may occur within minutes of administration of Survanta. Therefore, frequent and careful clinical observation and monitoring of systemic oxygenation are essential to avoid hyperoxia. Each dose of Survanta is 100 mg of phospholipid / kg birth weight (4 mL/kg). The Survanta Dosage Chart shows the total dosage for a range of birth weights.

The dosing chart for Survanta is presented in Table 1 below.

Dosage

Four doses of Survanta can be administered in the first 48 hours of life. Doses should be given no more frequently than every 6 hours.

Table 1

SURVANTA DOSING CHART			
WEIGHT (grams)	**TOTAL DOSE (mL)**	**WEIGHT (grams)**	**TOTAL DOSE (mL)**
600 - 650	2.6	1301 - 1350	5.4
651 - 700	2.8	1351 - 1400	5.6
701 - 750	3.0	1401 - 1450	5.8
751 - 800	3.2	1451 - 1500	6.0
801 - 850	3.4	1501 - 1550	6.2
851 - 900	3.6	1551 - 1600	6.4
901 - 950	3.8	1601 - 1650	6.6
951 - 1000	4.0	1651 - 1700	6.8
1001 - 1050	4.2	1701 - 1750	7.0
1051 - 1100	4.4	1751 - 1800	7.2
1101 - 1150	4.6	1801 - 1850	7.4

SURVANTA DOSING CHART			
WEIGHT (grams)	**TOTAL DOSE (mL)**	**WEIGHT (grams)**	**TOTAL DOSE (mL)**
1151 - 1200	4.8	1851 - 1900	7.6
1201 - 1250	5.0	1901 - 1950	7.8
1251 - 1300	5.2	1951 - 2000	8.0

Directions for Use

Survanta should be inspected visually for discolouration prior to administration. The colour of Survanta is off-white to light brown. If settling occurs during storage, swirl the vial gently (DO NOT SHAKE) to redisperse. Some foaming at the surface may occur during handling and is inherent in the nature of the product.

Survanta is stored refrigerated (2 - 8°C). Before administration, Survanta should be warmed by standing at room temperature for at least 20 minutes or warmed in the hand for at least 8 minutes. ARTIFICIAL WARMING METHODS SHOULD NOT BE USED. If a prevention dose is to be given, preparation of Survanta should begin before the infant's birth.

Unopened, unused vials of Survanta that have been warmed to room temperature may be returned to the refrigerator within 8 hours of warming and stored for future use. Drug should not be warmed and returned to the refrigerator more than once. Each single-use vial of Survanta should be entered only once. Used vials with residual drug should be discarded.

SURVANTA DOES NOT REQUIRE RECONSTITUTION OR SONICATION BEFORE USE.

Dosing Precautions

If an infant experiences bradycardia or oxygen desaturation during the dosing procedure, stop the dosing procedure and initiate appropriate measures to alleviate the condition. After the infant has stabilised, resume the dosing procedure.

Rales and moist breath sounds can occur transiently after administration of Survanta. Endotracheal suctioning or other remedial action is unnecessary unless clear-cut signs of airway obstruction are present.

Methods of administration

Method A outlined below was the original method of administration in all the controlled clinical studies that established the efficacy and safety of Survanta.

The two additional methods of administering Survanta were compared to the original method in a multi-centre, randomised clinical trial involving 299 infants weighing 600 g or more with RDS requiring mechanical ventilation. There were no significant differences among the three methods in

average FiO_2 a/A PO_2 or MAP at 72 hours of age, or in the incidence of pulmonary air leaks, pulmonary interstitial emphysema, patent ductus arteriosus, or mortality at 72 hours of age.

Method B, keeping the infant on the ventilator is considered the delivery method of choice as it was associated with less clinical deterioration (expressed as falls in heart rate and in oxygen saturation) during and immediately following treatment. Method B was associated with a greater degree of Survanta reflux than the other methods. This reflux was not associated with any clinical consequence.

Method A: Instillation through end-hole catheter - Disconnection from the ventilator.

Survanta is administered intratracheally by instillation through a 5 French end-hole catheter inserted into the infant's endotracheal tube with the tip of the catheter protruding just beyond the end of the endotracheal tube above the infant's carina. Before inserting the catheter through the endotracheal tube, the length of the catheter should be shortened. Survanta should not be installed into a main-stream bronchus.

It is important to ensure homogenous distribution of Survanta through the lungs. In the controlled clinical trials, each dose was divided into four quarter doses. Each quarter-dose was administered with the infant in a different position.

The sequence of positions was:

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

First Dose

Determine the total dose of Survanta from the Survanta Dosing Chart based on the infant's birth weight. Slowly withdraw the entire contents of the vial into a plastic syringe through a large-gauge needle (e.g. at least 20 gauge). DO NOT FILTER SURVANTA AND AVOID SHAKING.

Attach the premeasured 5 French end-hole catheter to the syringe. Fill the catheter with Survanta.

BEFORE ADMINISTERING Survanta, assure proper placement and patency of the endotracheal tube. At the discretion of the clinician, the endotracheal tube may be suctioned before administering Survanta. The infant should be allowed to stabilise before proceeding with dosing.

In the prevention strategy, weigh, intubate and stabilise the infant. Administer the dose as soon as possible after birth, preferably within 15 minutes. Position the infant appropriately and gently inject the first quarter-dose through the catheter over 2-3 seconds.

After administration of the first quarter-dose, remove the catheter from the endotracheal tube. Manually ventilate with a hand-bag with sufficient oxygen to prevent cyanosis, at a rate of 60 breaths/minute, and sufficient positive pressure to provide air exchange and chest wall excursion.

In the rescue strategy, the first dose should be given as soon as possible after the infant is placed on a ventilator for management of RDS. In the clinical trials, immediately before instilling the first quarter-dose, in infants ventilator settings were changed to rate 60/minute, inspiratory time 0.5 second, and FiO_2 1.0.

Position the infant appropriately and gently inject the first quarter-dose through the catheter over 2-3 seconds. After administration of the first quarter-dose, remove the catheter from the endotracheal tube. Return the infant to the mechanical ventilator.

In both strategies, ventilate the infant for at least 30 seconds or until stable. Reposition the infant for instillation of the next quarter-dose.

Instil the remaining quarter-doses using the same procedures. After instillation of each quarter-dose, remove the catheter and ventilate for at least 30 seconds or until the infant is stabilised. After instillation of the final quarter-dose, remove the catheter without flushing it. Do not suction the infant for 1 hour after quarter dosing unless signs of significant airway obstruction occur.

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

<u>Method B: Instillation through the secondary lumen of a double-lumen endotracheal tube - No disconnection from the ventilator.</u>

Survanta can be given by inserting the 5 French end-hole catheter through a neonatal suction valve WITHOUT DISCONNECTING THE ENDOTRACHEAL TUBE FROM THE VENTILATOR.

Survanta can also be instilled through the secondary lumen of a double-lumen endotracheal tube. The administration of Survanta using a double-lumen endotracheal tube is functionally equivalent to the use of the neonatal suction valve; i.e. delivery of Survanta at the distal end of the endotracheal tube without interrupting mechanical ventilation. If an infant is already intubated with a single-lumen endotracheal tube, the infant should not be reintubated with a double-lumen endotracheal tube solely for the purposes of administering Survanta.

To ensure homogeneous distribution of Survanta through the lungs, each dose is divided into fractional doses. Each dose can be administered in four quarter-doses as described in Method A above or in two half-doses.

To administer Survanta in two half-doses, the sequence of positions is:

- Head and body turned approximately 45° to the right
- Head and body turned approximately 45° to the left

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

The procedure for dosing is similar to Method A, the only differences being the administration of two half-doses instead of four quarter-doses and no disconnection of the endotracheal tube from the ventilator.

First Dose

BEFORE ADMINISTERING SURVANTA. Ensure proper placement and patency of the endotracheal tube. At the discretion of the clinician, the endotracheal tube may be suctioned before administering Survanta. The infant should be allowed to stabilise before proceeding with dosing.

In the prevention strategy, weigh, intubate and stabilise the infant. Administer the dose as soon as possible after birth, preferably within 15 minutes. Attach the syringe containing Survanta to the secondary lumen. Position the infant with the head and body turned approximately 45° to the right and gently inject the first fractional dose through the secondary lumen over 2-3 seconds without interrupting ventilation. If manually ventilated, ventilate with a hand-bag with sufficient oxygen to prevent cyanosis, at a rate of 60 breaths/minute, and sufficient positive pressure to provide adequate air exchange and chest wall excursion.

In the rescue strategy, the first dose should be given as soon as possible after the infant is placed on a ventilator for management of RDS. Immediately before instilling the first fractional dose, change the infant's ventilator settings to rate 60/minute, inspiratory time 0.5 second, and FiO_2 1.0.

Position the infant appropriately, i.e. head and body turned approximately 45° to the right, and gently inject the first fractional dose through the secondary lumen over 2-3 seconds without interrupting mechanical ventilation.

In both strategies, ventilate the infant for at least 30 seconds or until stable. Reposition the infant for instillation of the next fractional dose.

Instil the remaining fractional doses using the same procedures. After instillation of each fractional dose, ventilate for at least 30 seconds or until the infant is stabilised. After instillation of the final fractional dose, remove the syringe from the secondary lumen. INJECT 0.5 mL OF AIR TO FLUSH THE SECONDARY LUMEN AND CAP IT.

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

Method C

Survanta can be administered by inserting the 5 French catheter through the endotracheal tube while the endotracheal tube is briefly disconnected from the ventilator. The half doses were administered in the two positions described as for Method B.

The procedure for dosing is similar to Method A, the only difference being the use of two half doses instead of four quarter doses.

With the infant supine, the head and body of the infant were turned approximately 45° to the right. The infant is removed from the ventilator and the primed catheter inserted into the endotracheal tube. The first half of the Survanta is then delivered and the catheter withdrawn. The infant is then returned to the ventilator for at least 30 seconds of mechanical ventilation.

The head and body of the infant is turned approximately 45° to the left. The second half dose of Survanta is delivered in the same manner as the first. The catheter is withdrawn and the infant returned to mechanical ventilation.

Repeat doses (all methods)

The dosage of Survanta for repeat doses is also 100 mg phospholipid/kg and is based on the infant's birth weight. The infant should not be reweighed for determination of the Survanta dosage. Use the Survanta Dosing Chart to determine the total dosage.

The need for additional doses of the Survanta is determined by evidence of continuing respiratory distress. Using the following criteria for redosing, significant reductions in mortality due to RDS were observed in the multiple-dose clinical trials with Survanta.

Dose no sooner than 6 hours after the preceding dose if the infant remains intubated and requires at least 30% inspired oxygen to maintain a PaO2 less than or equal to 80 torr.

Radiographic confirmation of RDS should be obtained before administering additional doses to those who received a prevention dose.

Prepare Survanta and position the infant for administration of each fractional dose as previously described. After instillation of each fractional dose, remove the dosing catheter from the endotracheal tube (Method A) and ventilate the infant for at least 30 seconds or until stable.

In the clinical studies, ventilator settings used to administer repeat doses were different than those used for the first dose. For repeat doses, the FiO_2 was increased by 0.20 or an amount sufficient to prevent cyanosis. The ventilator delivered a rate of 30/minute with an inspiratory time less than 1.0 second. If the infant's pretreatment rate was 30 or greater, it was left unchanged during Survanta instillation.

Manual hand-bag ventilation should not be used to administer repeat doses. DURING THE DOSING PROCEDURE, VENTILATOR SETTINGS MAY BE ADJUSTED AT THE DISCRETION OF THE CLINICIAN TO MAINTAIN APPROPRIATE OXYGENATION AND VENTILATION.

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

4.3 Contraindications

None known.

4.4 Special warnings and precautions for use

Survanta is intended for intratracheal use only.

SURVANTA CAN RAPIDLY AFFECT OXYGENATION AND LUNG COMPLIANCE. Therefore, its use should be restricted to a highly supervised clinical setting with immediate availability of clinicians experienced with intubation, ventilator management and general care of premature infants. Infants receiving Survanta should be frequently monitored with arterial or transcutaneous measurement of systemic oxygen and carbon dioxide.

DURING THE DOSING PROCEDURE, TRANSIENT EPISODES OF BRADYCARDIA AND DECREASED OXYGEN SATURATION HAVE BEEN REPORTED. If these occur, stop the dosing procedure and initiate appropriate measures to alleviate the condition. After stabilisation, resume the dosing procedure.

General

Rales and moist breath sounds can occur transiently after administration. Endotracheal suctioning or other remedial action is not necessary unless clear-cut signs of airway obstruction are present.

Increased probability of post-treatment nosocomial sepsis in Survanta-treated infants was observed in the controlled clinical trials (See Table 2). The increased risk for sepsis among Survanta-treated infants was not associated with increased mortality among these infants. The causative organisms

were similar in treated and control infants. There was no significant difference between groups in the rate of post-treatment infections other than sepsis.

Use of Survanta in infants less than 600 g birth weight or greater than 1750 g birth weight has not been evaluated in controlled trials. There is no controlled experience with use of Survanta in conjunction with experimental therapies for RDS (e.g. high-frequency ventilation or extracorporeal membrane oxygenation).

No information is available on the effects of doses other than 100 mg phospholipids / kg, more than four doses, dosing more frequently than every 6 hours, or administration after 48 hours of age.

Use in the elderly

Survanta is indicated for use in premature infants. There are no data in elderly subjects.

Paediatric use

Survanta is indicated for use in premature infants. Refer to the details included in the general section above.

Effects on laboratory tests

In the controlled clinical trials, there was no effect of Survanta on results of common laboratory tests: white blood cell count and serum sodium, potassium, bilirubin, creatinine.

4.5 Interactions with other medicines and other forms of interactions

No data available.

4.6 Fertility, pregnancy and lactation

Effects on fertility

Reproduction studies in animals have not been completed.

Use in pregnancy

Survanta is indicated for use in premature infants. There are no data available on the use of Survanta in pregnancy.

Use in lactation

Survanta is indicated for use in premature infants. There are no data available on the use of Survanta in breastfeeding women.

4.7 Effects on ability to drive and use machines

Survanta is indicated for use in premature infants. The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (Undesirable effects)

The most commonly reported adverse experiences were associated with the dosing procedure. In the multiple-dose controlled clinical trials, transient bradycardia occurred with 11.9% of doses. Oxygen desaturation occurred with 9.8% of doses.

Other reactions during the dosing procedure occurred with less than 1% of doses and included endotracheal tube reflux, pallor, vasoconstriction, hypotension, endotracheal tube blockage, hypertension, hypocarbia, hypercarbia and apnoea. No deaths occurred during the dosing procedure, and all reactions resolved with symptomatic treatment.

The occurrence of concurrent illnesses common in premature infants was evaluated in the controlled trials. The rates in all controlled studies are presented in Table 2 below.

Table 2

	All Controlled Studies		
Concurrent Event	**Survanta (%)**	**Control (%)**	**p-Value***
Patent ductus arteriosus	46.9	47.1	0.814
Intracranial haemorrhage	48.1	45.2	0.241
Severe intracranial haemorrhage	24.1	23.3	0.693
Pulmonary air leaks	10.9	24.7	<0.001
Pulmonary interstitial emphysema	20.2	38.4	<0.001
Necrotizing enterocolitis	6.1	5.3	0.427
Apnoea	65.4	59.6	0.283
Severe apnoea	46.1	42.5	0.114
Post-treatment sepsis	20.7	16.1	0.019
Post-treatment infection	10.2	9.1	0.345
Pulmonary haemorrhage	7.2	5.3	0.156

*p-Value comparing groups in controlled studies

When all controlled studies were pooled, there was no difference in intracranial haemorrhage. However, in one of the single-dose rescue studies and one of the multiple-dose prevention studies,

the rate of intracranial haemorrhage was significantly higher in Survanta patients than control patients (63.3% v 30.8%, p=0.001 and 48.8% v 34.2%, p=0.047).

More than 3700 pre-treatment and post-treatment serum samples were tested by Western Blot immunoassay for antibodies to surfactant-associated proteins SP-B and SP-C. No IgG or IgM antibodies were detected.

Several other complications are known to occur in premature infants. The following conditions were reported in the controlled clinical studies. The rates of the complications were not different in treated and control infants, and none of the complications were attributed to Survanta.

Respiratory: lung consolidation, blood from the endotracheal tube, deterioration after weaning, respiratory decompensation, subglottic stenosis, paralysed diaphragm, respiratory failure.

Cardiovascular: hypotension, hypertension, tachycardia, ventricular tachycardia, aortic thrombosis, cardiac failure, cardio-respiratory arrest, increased apical pulse, persistent foetal circulation, air embolism, total anomalous pulmonary venous return.

Gastrointestinal: abdominal distension, haemorrhage, intestinal perforations, volvulus, bowel infarct, loading intolerance, hepatic failure, stress ulcer.

Renal: renal failure, haematuria.

Haematologic: coagulopathy, thrombocytopenia, disseminated intravascular coagulation.

Central Nervous System: seizures.

Endocrine/Metabolic: adrenal haemorrhage, inappropriate ADH secretion, hyperphosphataemia.

Musculoskeletal: inguinal hernia.

Systemic: fever, deterioration.

Follow-Up Evaluations

To date, no long-term complications or sequelae of Survanta therapy have been found.

Single-Dose Studies

Six-month adjusted-age follow-up evaluation of 232 infants (115 treated) demonstrated no clinically important differences between treatment groups in pulmonary and neurologic sequelae, incidence or severity of retinopathy of prematurity, rehospitalisations, growth, or allergic manifestations.

Multiple-Dose Studies

Six-month adjusted age follow-up evaluations have not been completed. Preliminarily, in 605 (333 treated) of 916 surviving infants, there are trends for decreased cerebral palsy and need for supplemental oxygen in Survanta infants. Wheezing at the time of examination tended to be more frequent among Survanta infants, although there was no difference in bronchodilator therapy.

Twelve-month follow-up data from the multiple-dose studies have been completed in 328 (171 treated) of 909 surviving infants. To date no significant differences between treatments have been found, although there is a trend toward less wheezing in Survanta infants in contrast to the six month results.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 Overdose

Overdosage with Survanta has not been reported.

Based on animal data, overdosage might result in 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 suctioning or other remedial action is not required unless clear-cut signs of airway obstruction are present.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Endogenous pulmonary surfactant lowers surface tension on alveolar surfaces during respiration and stabilises the alveoli against collapse at resting transpulmonary pressures. Deficiency of pulmonary surfactant causes Respiratory Distress Syndrome (RDS) in premature infants. Survanta replenishes surfactant and restores surface activity to the lungs of these infants.

Activity

In vitro, Survanta reproducibly lowers minimum surface tension to less than 8 dynes/cm on the pulsating bubble surfactometer and Wilhelmy Surface Balance.

In vivo, single Survanta doses improve lung pressure-volume measurements, lung compliance, and oxygenation in premature rabbit and sheep.

Clinical trials

Clinical effects of Survanta were demonstrated in six single-dose and four multiple-dose randomised, multicentre, controlled clinical trials involving approximately 1700 infants. Three open trials involved more than 4800 infants. Each dose of Survanta in all studies was 100 mg phospholipids / kg birth weight.

Prevention Studies

Infants of 600-1250 g birth weight and 23 to 29 weeks estimated gestational age were enrolled in two multiple-dose studies. A dose of Survanta was given within 15 minutes of birth to prevent the development of RDS. Up to three additional doses in the first 48 hours, as often as every 6 hours, were given if RDS subsequently developed.

Rescue Studies

Infants of 600-1750 g birthweight, with RDS requiring mechanical ventilation and an $FiO_2 \geq 0.40$ were enrolled in two multiple-dose rescue studies. The initial dose of Survanta was given after RDS developed and before 8 hours of age. Infants could receive up to three additional doses in the first 48 hours, as often as every 6 hours.

5.2 Pharmacokinetic properties

The metabolic disposition of Survanta in humans has not been studied. In animal experiments using premature rabbit and sheep models, the metabolic fates of isotope-labelled phosphatidylcholine, palmitic acid and tripalmitin were characterised. Clearance of these components occurs in two phases: clearance from alveolar airspaces and subsequent clearance from the lung tissue. In premature sheep, the labelled phosphatidylcholine in Survanta and natural sheep surfactant were cleared equivalently from the alveolar airspaces with only about 20% of the administered dose recovered in alveolar washes at 24 hours. There was little or no clearance from the lungs for either surfactant. These isotope experiments showed that the labelled phosphatidylcholine in Survanta entered endogenous surfactant phosphatidylcholine metabolic pathways and was recycled back to the airspaces for reutilisation. In premature rabbits, airspace clearance was similar for Survanta,

natural calf surfactant and natural rabbit surfactant, although there was less lung clearance of Survanta than the natural surfactants.

In contrast to the phosphatidylcholine in Survanta, labelled palmitic acid was rapidly cleared from both the airspaces and the lungs of premature rabbits and sheep. Some of the palmitate was incorporated into lung lipid, primarily phosphatidylcholine, while much of the palmitate left the lungs. The tripalmitin in Survanta distributed to the airspaces and lung tissue of premature sheep similarly to phosphatidylcholine.

Limited animal experiments have not found effects of Survanta on endogenous surfactant metabolism. Precursor incorporation and subsequent secretion of saturated phosphatidylcholine in premature sheep were not changed by either natural surfactant or Survanta treatments. However, when the intra-animal variability was minimised by comparing a treated to an untreated lung in the same animal, natural surfactant stimulated both precursor incorporation and secretion in adult rabbits. Survanta stimulated endogenous surfactant secretion alone, and the effect was not as large as for natural surfactant.

5.3 Preclinical safety data

Genotoxicity

Mutagenicity studies were negative.

Carcinogenicity

Carcinogenicity studies have not been performed with Survanta.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Refer to section 2 – QUALITATIVE AND QUANTITATIVE COMPOSITION.

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store unopened vials at refrigeration temperature (2-8°C). Protect from light. Store vials in carton until ready for use. Vials are for single use only. Upon opening, discard unused drug.

6.5 Nature and contents of container

Survanta (beractant) intratracheal suspension is supplied in single-use clear glass vials with chlorobutyl grey rubber stopper and a 20 mm flip off Al cap containing 8 mL of Survanta; packs of 1 x 8 mL vials.

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical properties

Chemical structure

Chemical structure not available.

CAS number

108778-82-1

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine - Schedule 4

8 SPONSOR

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241 O'Riordan Street
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Australia
Tel: 1800 043 460

9 DATE OF FIRST APPROVAL

18 March 1994

10 DATE OF REVISION

21 May 2019

Summary table of changes

Section Changed	Summary of new information
All sections	Reformat to align with revised TGA PI requirements
All sections	Minor editorial changes including correction of typographical errors, conversion to Australian spelling and grammatical corrections.