care units with suitable equipment.
A small percentage of patients do not react with the first dose. In such cases, it is suggested discarding other pathologies, like cardiorespiratory diseases.
The partial arterial oxygen pressure and the pulmonary expansion should be constantly monitored since, frequently, the fraction of inspired oxygen and/or the ventilation pressures used before the administration of the medicine should be diminished, to prevent the risk of causing a pulmonary interstitial disease, air escapes and/or pulmonary hyperinsuflation, hypotension, cerebral hemorrhage, pneumothorax, apnea and early infectious pathologies associated.
It is advised to take thorax x-rays 30 to 60 minutes after each dose, to control the pulmonary ventilation and expansion.
The modifications in the parameters of mechanical respiratory assistance should begin about 10 minutes after finalizing the administration of the surfactant; if required, gases in blood, monitoring, thorax x-ray, etc. can be controlled later.
The most distinct effect of the treatment is the immediate improvement in oxygenation, allowing rapid reductions in FiO2 that can reach, in some cases, up to 0.21 in few minutes. Compliance development usually shows a favorable trend from the beginning of the treatment, although it is more gradual in FiO2.
Respirator pressure should be cautiously changed, diminishing the inspiratory pressure (PIM) before the expiratory (PEEP) pressure, and maintaining the latter values between 4 and 6 cm of water, until 36 to 48 hours after birth, according to clinic and gasometry results.
There is a variable percentage of patients who do not respond to treatment, either because the respiratory disorder is not caused by surfactant deficiency, or due to the presence of any other associated factor that inhibits the action of the treatment.
It is recommended not to aspirate the airway within the hour subsequent to the tracheal instillation, unless there is evidence of significant obstruction.
Rales and crepitations can occur during the administration. The use of Surfactant Richet B is not related to an increase of in-hospital sepsis.
So far, there has not been any report about the use of doses other than 100 mg/kg or more than four doses or any frequency higher than one dose every 6 hours or the administration after 48 hours of age.

■ **ADVERSE REACTIONS:**
With multiple doses, some cases of bradycardia, oxygen desaturation and hypotension have been reported.
In some cases, endotracheal reflux, blood vessel constriction, bradycardia, hypotension, endotracheal blockade, hypertension, hypocapnia, hypercapnia, and apnea detectable by constant monitoring of vital and clinical signs and gasometry have been reported.
No variations have been observed in laboratory study results (count of white blood cells, sodium, potassium, bilirubin and creatinine). No increase has been observed in IgG or IgM.
After the treatment, TET may become acutely obstructed due to secretions or the surfactant (in these cases, the TET is aspirated or changed); sub acute and transient obstruction of upper airways can occur, with a moderate increase in PCO2, that is reverted spontaneously. Other possible reactions are: hypotension during or in the last minutes of treatment, that, if persisting for over 15 to 30 minutes, is solved by means of specific treatment; hyperventilation of a lung or lobe with hyperventilation of the rest if Surfactant instillation was done beyond the trachea by error (in these cases, it is recommended to apply a new dose with the patient in contralateral position to the one that was hyperventilated, even though there are few possibilities of success); early opening of ductus arteriosus; pulmonary hemorrhage, which is a low frequent complication but with a high mortality rate, for which treatment it is recommended to increase PEEP and to aspirate the airways frequently, adjusting ARM parameters.

■ **OVERDOSAGE:**
In the event of overdosage, go to the nearest hospital or contact Toxicology Centers at:
Pediatrics Hospital Ricardo Gutiérrez (011) 4962-6666 / 2247
Alejandro Posadas Hospital (011) 4654-6648 / 4658-7777
Optionally contact other toxicological centers.

■ **HOW SUPPLIED:**
Packages containing a vial with:
3 ml (90 mg of Bovine Lung Surfactant)
4 ml (120 mg of Bovine Lung Surfactant)
8 ml (200 mg of Bovine Lung Surfactant)
8 ml (240 mg of Bovine Lung Surfactant)

■ **STORAGE AND CONSERVATION MODE:**
Keep in refrigerator (between 2º C and 8º C)

KEEP MEDICINAL PRODUCTS OUT OF REACH OF CHILDREN

Medical specialty authorized by the Argentine Ministry of Health
Certificate Nº 49004

Technical Director: HORACIO R. LANCELLOTTI - Pharmacist

Cd: 00.000/rev01
Act: 08/2012 T.3

Manufactured by LABORATORIOS RICHET S.A.
Terrero 1251/53/59 - Buenos Aires, Argentina
Phone number: (54-11) 4585-555 - Fax number: (54-11) 4584-1593

MADE IN ARGENTINA

RICHET

Bovine Lung Surfactant
Surfactant Richet B®

Intratracheal suspension

SOLD BY PRESCRIPTION - RX ONLY

■ **FORMULA:**
Each vial contains:
Surfactant Richet B 90 mg (30 mg/ml):
Bovine lung surfactant……90 mg
Physiological solution q.s……3 ml
Surfactant Richet B 120 mg (30 mg/ml):
Bovine lung surfactant……120 mg
Physiological solution q.s……4 ml
Surfactant Richet B 200 mg (25 mg/ml):
Bovine lung surfactant……200 mg
Physiological solution q.s……8 ml
Surfactant Richet B 240 mg (30 mg/ml):
Bovine lung surfactant……240 mg
Physiological solution q.s……8 ml

■ **THERAPEUTIC ACTION:**
Surfactant Richet B replaces the surfactant and re-establishes the surface tension value in the pulmonary alveoli of premature infants.

■ **INDICATIONS:**
Surfactant Richet B is indicated for the prevention and treatment of the Respiratory Distress Syndrome (RDS or Hyaline Membrane Syndrome) in premature infants, reducing the incidence, mortality and complications caused by this syndrome.

■ **PHARMACOLOGICAL CHARACTERISTICS/PROPERTIES:**
Pharmacological action:
Endogenous lung surfactant lowers surface tension on pulmonary alveoli during respiration, stabilizes alveoli and prevents lungs from collapsing at resting transpulmonary pressure.
Deficiency of lung surfactant results in Respiratory Distress Syndrome (RDS) in premature infants.
Surfactant Richet B replenishes surfactant and restores surface activity to the lungs of premature infants.

Pharmacokinetics:
Surfactant Richet B is administered directly to the target organ, i.e. the lungs, where biophysical effects occur at the alveolar surface.
In surfactant-deficient premature rabbits and lambs, alveolar clearance of the isotopically marked compounds is rapid. A high proportion of the dose becomes lung-associated within hours and the lipids enter the endogenous surfactants pathway of reutilization and recycling.
In surfactant-sufficient adult animals, clearance is faster than in premature and young animals, because there is less reutilization and recycling of surfactant in adult animals.
Limited tests on animals have shown that these surfactants do not have any effect on endogenous surfactant metabolism. Precursor incorporation and the subsequent secretion of saturated phosphatidylcholine in premature sheep are not modified by surfactant treatments.

■ POSOLOGY/DOSAGE AND ADMINISTRATION METHODS:

Surfactant Richet B is intended for intratracheal use only. It should not be administered by intravenous, intramuscular or transdermal injection. Always use sterile supply and maintain aseptic conditions.
Surfactant Richet B should be administered by or under the supervision of physicians with experience in intubation, ventilation and general care of premature infants, in neonatal intensive care units, with constant monitoring of vital functions.
Posology:
The suggested average posology is 100 mg/kg of weight at birth, as shown in the following dosing chart:

Weight in	Dose in ml		Weight in	Dose in ml	
grams	30 mg/ml	25 mg/ml	grams	30 mg/ml	25 mg/ml
600 - 650	2.16	2.59	1301 – 1350	4.50	5.40
651 - 700	2.33	2.80	1351 – 1400	4.66	5.59
701 - 750	2.50	3.00	1401 – 1450	4.83	5.80
751 - 800	2.66	3.19	1451 – 1500	5.00	6.00
801 - 850	2.83	3.40	1501 – 1550	5.16	6.19
851 - 900	3.00	3.60	1551 – 1600	5.33	6.40
901 - 950	3.16	3.79	1601 – 1650	5.50	6.60
951 - 1000	3.33	4.00	1651 – 1700	5.83	7.00
1001 - 1050	3.50	4.20	1701 – 1750	6.00	7.20
1051 - 1100	3.66	4.39	1751 – 1800	6.16	7.39
1101 - 1150	3.83	4.60	1801 – 1850	6.33	7.60
1151 - 1200	4.00	4.80	1851 – 1900	6.50	7.80
1201 - 1250	4.16	4.99	1901 – 1950	6.66	7.99
1251 - 1300	4.33	5.20	1951 – 2000	6.83	8.20

It can be administered in a single dose or it can be divided into four doses to be distributed throughout the first 48 hours of life, with a frequency not higher than one every 6 hours.
As the product should be stored refrigerated between 2º and 8º C, before administration the vial should be warmed at room temperature for at least 20 minutes or in the hand for about 8 minutes. Under no circumstance should it be artificially warmed.
If the vial remains closed outside the refrigerator for less than 8 hours, it may be returned to the refrigerator, but that operation cannot be repeated. Once opened, any unused portion should be discarded.
Surfactant Richet B should not be instilled into the mainstem bronchi.
A double-lumen endotracheal tube enables to administer the surfactant without disconnecting the patient from mechanical or manual ventilation. The procedure is easier if one person holds the baby and another one administers the dose. The surfactant can be administered in aliquots or by slow push (10 minutes).
It is important to assure the homogenous distribution of the surfactant in the lungs. For that, each dose is divided into quarters, and each quarter-dose is administered with the infant in different positions, according to the following sequence:
• Its head and body slightly leaning downwards, and its head turning to the right.
• Its head and body slightly leaning downwards, and the head turning to the left.
• Its head and body slightly leaning upwards, and the head turning to the right.
• Its head and body slightly leaning upwards, and the head turning to the left.

First dose:
If a double-lumen endotracheal tube is not available, a K35 catheter with a distal orifice, through a conventional endotracheal tube can be used.
The dose can be divided into four equal parts that will be administered at one-minute intervals, during which oxygen is supplied.
During administration, partial arterial oxygen pressure should be monitored to prevent hypoxaemia during the procedure or hyperoxia after the procedure.
If the surfactant is used for prevention purposes in the delivery room, mainly prior to the first breathing, it can be administered in a single dose, through a double-lumen endotracheal tube, by push over 5 minutes, ventilating the patient with a neonatal resuscitator bag containing oxygen, with a pressure gauge and vital signs monitoring.

Repeat doses:
The surfactant dose for repeat administration is also 100 mg of phospholipid/kg of weight at birth. It is not necessary to weigh the infant again to adjust the dose.
The need for any additional dose is determined by evidence of continuing respiratory distress. The usual criteria applied is the following:
Do not administer new doses sooner than 6 hours after the preceding dose, if the infant remains intubated and requires at least 30% of inspired oxygen to maintain a PaO2 smaller or equal to 80 torr.
Radiographic confirmation of RDS should be obtained before administering additional doses to those who received a prevention dose.
In the rescue strategy, the first dose should be given as soon as possible after the infant is placed on a ventilator for treatment of Respiratory Deficiency Syndrome. The parameters used have been a rate of 60 breathing/minute with an inspiratory time at 0.5 seconds and FiO2 according to the value of gases in blood.
Position the infant appropriately and gently inject the first quarter-dose through the catheter over 2-3 seconds; then, remove the catheter while continuing with the mechanical or manual ventilation with ambu bag with oxygen for 3 minutes.
In any strategy, the manual ventilation lasts at least 180 seconds or until the infant is stabilized. Reposition the infant and administer the other quarter-dose, using for that dose and the following the same technique. After each quarter-dose the catheter is withdrawn and ventilation should be applied for at least 30 seconds or until the infant is stabilized.
After administering the last quarter-dose, the catheter is withdrawn, not allowing the liquid to flow if there is not a double-lumen endotracheal tube properly located in the tracheal bifurcation. Do not suction the infant for 1 hour after dosing, unless there are signs of significant airway obstruction. Once the procedure has been completed, ventilation and clinical care are resumed modifying the respirator's parameters, according to the oximetry and gasometry levels.
When repeat doses are administered, the total amount to administer is the same that in the previous case. If other pathologies have been discarded and the respiratory difficulty continues, additional doses are administered.
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 PaO lower than or equal to 80 torr.
Before administering new doses, other pathologies should be discarded, even by x-ray. After the administration of each quarter-dose, the endotracheal tube catheter is withdrawn while continuing with manual ventilation for at least 180 seconds or until the infant is clinically stabilized.
As in the previous case, after completing the dosage, resume ventilation and clinical procedures, adapting the respirator parameters to the values obtained by oximetry and gasometry.

Dosage precautions:
If the newborn develops bradycardia or oxygen desaturation during the dosage procedure, the treatment is suspended and suitable measures are applied to revert the condition. Once the patient is stabilized, the dosing procedure is resumed.
Transient rales or moist breath sounds can occur after the administration of Surfactant Richet B. It is not necessary to perform endotracheal aspiration or any other therapeutic procedure, unless there are clear signs of airway obstruction.

■ CONTRAINDICATIONS:

Not described so far.

■ WARNINGS:

Surfactant Richet B is intended for intratracheal use only.
The administration of Surfactant Richet B requires experience in this type of procedures.
Patients should be permanently 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 any of such situations occurs, stop the dosing procedure and initiate appropriate measures to alleviate the condition. After stabilization, resume the dosing procedure.
Constant clinical control and an early echocardiograph should be performed for the appearance of ductus arteriosus.
The use of Surfactant Richet B in infants that weigh less than 600 g or more than 1950 g has not been effectively evaluated in controlled trials. There is no controlled evaluation of the use of Surfactant Richet B in conjunction with experimental therapies, like high frequency ventilation or extracorporeal membrane oxygenation.
There is no information regarding the use of any dose higher than 100 mg/kg or administration of more frequent doses or administration in children older than 48 hours of life.

Carcinogenesis, mutagenesis, impairment of fertility:
Mutagenicity and carcinogenicity tests are negative.
It has been observed that rats dosed with 500 mg of subcutaneous phospholipids/kg/day, for 5 days, reproduce normally and there have been no adverse effects in the offspring.

■ PRECAUTIONS:

This product is intended to be used in hospital institutions by trained health care professionals, with experience in care and resuscitation of premature infants, in neonatal intensive