



CLINICAL PRACTICE GUIDELINE

Guideline coverage includes NICU KEMH, NICU PMH and NETS WA

Surfactant Therapy

This document should be read in conjunction with the [Disclaimer](#)

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Aim

This document covers two salient aspects of surfactant therapy in neonates.

- Indications for surfactant therapy in neonates.
- Type of surfactant: Poractant (Curosurf) or Beractant (Survanta).

Purpose and Definitions

Surfactant therapy is given to minimise atelectasis and reduce the work of breathing. This outcome is achieved by reducing the surface tension and promoting alveolar stability during expiration.

Prophylactic surfactant administration is considered to be treatment in the delivery room before or shortly after the first breath. A single dose of exogenous surfactant should be administered preferably within 15 minutes of birth.

Indications

- Mechanical ventilation for respiratory distress syndrome (RDS) and meconium aspiration syndrome (MAS).
- Consider in ventilated neonates with pulmonary haemorrhage.
- Consider in ventilated neonates with severe RSV bronchiolitis.

For all indications, Survanta is the most cost-effective and hence preferred surfactant preparation within the NICU, except in extremely preterm infants (≤ 25 weeks) where Curosurf is to be used.

Refer to the [Neonatal Medication Protocols](#) for details of the dose and method of administration of surfactant, [Survanta](#) / [Curosurf](#).

Key Points

- Administration of surfactant is a dynamic treatment process involving prophylactic and responsive changes to mechanical ventilation alongside administration of the surfactant.
- Medical Staff should be present immediately before, during and for at least the first 5 minutes after surfactant administration to alter ventilation settings as required (ventilator rate, peak inspiratory pressure, FiO₂ and inspiratory time settings).
- Bolus administration of surfactant induces a transient marked increase in airway resistance that may precipitate airway occlusion, bradycardia and hypoxia. Judicious precautionary increases in driving pressure (PIP) and inspiratory time prior to surfactant administration and continuous adjustment of these parameters in response to flow monitoring and/or observation of the surfactant fluid column in the tracheal tube reduces the incidence and severity of this complication.
- Continuation of volume guarantee throughout the administration of surfactant (with retention of the flow sensor in the circuit) will ensure any increase in ventilator settings do not cause additional lung damage.
- Infants who receive surfactant in the delivery suite should be commenced on volume guarantee as soon as they arrive in the intensive care unit.
- Reassess ventilator settings every 15 minutes for an hour, then hourly thereafter. Note changes in SaO₂, V_T, and minute volume (MV). Reduce backup peak inspiratory pressure as required to ensure it remains 4-5 cmH₂O above the mean PIP required to achieve the targeted tidal volume.

- Curosurf improves oxygenation and lung compliance more rapidly than Survanta. Increase in lung volume is an indication of improved lung compliance. Reduction in ventilatory settings may be required within 5 minutes of administration.
- Adverse reactions to surfactant administration include transient hypoxia and bradycardia, endotracheal tube blockage and air leaks. Hypoxia and bradycardia are usually the result of tube blockage. If there is significant desaturation or bradycardia, stop the administration temporarily and make appropriate changes to the ventilator to ensure the surfactant fluid column in the tracheal tube advances distally and that flow is re-established.
- Surfactant administration is a minimum two-person procedure. The infant must have cardio-respiratory monitoring throughout. A third person is ideally present, with the sole responsibility for continuous adjustment of the ventilator during the procedure.

Equipment required

- Trachmac Device; size FG 5 for size 2, 2.5, 3, 3.5 endotracheal tubes
- Tracheal tube (size 2, 2.5, 3, 3.5 as required)
- Warmed surfactant (Survanta or Curosurf as determined by consultant)
- 10 mL syringe, drawing up needle and alcohol wipe
- Mechanical ventilator with flow-volume monitoring OR manual neonatal resuscitator

Administration

Surfactant administration in the delivery suite **WITHOUT** flow-volume monitoring

1. Place the infant in the supine position. The base of the warmer or incubator is to remain flat throughout.
2. Remove the blue connector from the endotracheal tube and attach the appropriate adaptor and Trachmac device. Reconnect endotracheal tube to ventilator.
3. Draw up the prescribed surfactant volume, add 1 mL of air. Ensure that the air is at the plunger end of the syringe. Attach syringe to luer lock connector of Trachmac.



1. The **insertion distance** for the Trachmac is determined by the length of the ETT to the cut off point plus 5 cm. (Note the colour band before the number for easier visualisation).
2. Insert the catheter & as soon as the colour appears in the “**window area**” of the Trachmac catheter - stop advancing the catheter (the tip will be at the end of the ETT to within 0.5 cm beyond the end of the ETT).
3. Instil ½ of dose over 5-10 s. Withdraw the trachmac catheter from the ETT as the peak inspiratory pressure is increased by 3 cmH₂O from pre-surfactant settings.
4. On or immediately after withdrawal of the Trachmac catheter administer 2 slow manual inflations (2-3 s) and observe the surfactant fluid column. If the fluid column does not move distally (toward the lung), increase peak inspiratory pressure by another 3 cmH₂O and repeat the 2 manual inflations until surfactant fluid column moves distally and chest rise/fall is observed (max 30 cmH₂O PIP).
5. Return to routine mechanical ventilation, wait until vital signs are stable, adjusting PIP and inspiratory time as surfactant is cleared and distributed to the lung. (inspiratory time will need to increase immediately after surfactant then decrease as fluid clears from the airway. Instil 2nd aliquot of surfactant followed by air to clear surfactant from catheter.
6. Withdraw the Trachmac catheter from the ETT as above and repeat manual inflation procedure as required.
7. Remove syringe and replace combi stop to connector.



1. Alter ventilator settings as medically ordered. Change to volume guarantee ventilation on transfer to a ventilator in the intensive care unit with PIP set at 4-5 cmH₂O above average PIP required to deliver target tidal volume.
2. Establish transcutaneous monitoring (T_{CM}) immediately after arrival in the intensive care unit. Confirm accuracy of T_{cp}CO₂ with a blood gas at ~15-30 minutes after administration to facilitate early recognition of over- or under-ventilation.
3. Subsequent blood gases as ordered.
4. Leave Trachmac device *in situ* for 2nd dose (if used) then discard.
5. Change to Ballard suction device after second administration of surfactant is complete.
6. Following administration, position prone if stable/practical.
7. Complete documentation.

Surfactant administration in the intensive care unit WITH flow-volume monitoring

1. Place the infant in the supine position. The base of the warmer or incubator is to remain flat throughout. Transcutaneous monitoring (TCM'S) advisable.
2. Leave flow sensor in place but keep elevated above the baby to reduce reflux of surfactant into the sensor (should be replaced after procedure if it becomes contaminated with surfactant).
3. Ensure the infant is on a volume targeted/volume-guarantee mode of ventilation and increase the backup PIP to at least 3 cmH₂O above the current required PIP to achieve target volume.
4. Remove the blue connector from the endotracheal tube and attach the appropriate adaptor and Trachmac device. Reconnect endotracheal tube to ventilator.
5. Draw up the prescribed surfactant volume, add 1 mL of air. Ensure that the air is at the plunger end of the syringe. Attach syringe to luer lock connector of Trachmac.



1. The **insertion distance** for the Trachmac is determined by the length of the ETT to the cut off point plus 5 cm. (Note the colour band before the number for easier visualisation).
2. Insert the catheter & as soon as the colour appears in the “**window area**” of the Trachmac catheter - stop advancing the catheter (the tip will be at the end of the ETT to within 0.5 cm beyond the end of the ETT).
3. Instil ½ of dose over 5-10 s. Withdraw the Trachmac catheter from the ETT.
4. As the Trachmac catheter is withdrawn, administer 2 slow manual inflations (2-3 s) via the ventilator and observe the surfactant fluid column. If the fluid column does not move distally (toward the lung), increase peak inspiratory pressure by another 3 cmH₂O and repeat the 2 manual inflations until surfactant fluid column moves distally and chest rise/fall is observed (max 30 cmH₂O PIP).
5. Allow routine ventilation to resume and confirm re-establishment of airflow with the flow monitoring. Adjust inspiratory time as required to ensure complete delivery of inspiratory flow (longer inspiratory times are required until the surfactant has cleared from the airways).
6. Wait until vital signs are stable.
7. Instil 2nd aliquot of surfactant followed by air to clear surfactant from catheter.
8. Withdraw the trachmac catheter from the ETT as above and repeat steps 4-6.
9. Remove syringe and replace combi stop to connector.



1. Adjust ventilator settings as medically ordered. Importantly, reduce maximum PIP as required to maintain it at pressures ~ 4-5 cmH₂O above the average PIP required to achieve the target tidal volume. Inspiratory time may also need to be adjusted.
2. Confirm accuracy of T_{cp}CO₂ with a blood gas at ~15-30 minutes after administration to facilitate early recognition of over- or under-ventilation.
3. Subsequent blood gases as ordered.
4. Leave Trachmac device *in situ* for 2nd dose if required then discard.

5. Change to Ballard suction device after second administration of surfactant is complete.
6. Following administration, position prone if stable/practical.
7. Complete documentation.

INTubate, SURfactant, Extubate (INSURE) Procedure

Indications

NOTE: INSURE method of administering surfactant is at the discretion of the on call consultant.

Any non-intubated infants with clinical signs of respiratory distress or other evidence of RDS like abnormal gas (respiratory acidosis), worsening FiO₂ requirement or abnormal CXR can be considered for the procedure.

- Eligible infants should have good respiratory effort
- Preferably less than 6 hours old (earlier the age of INSURE better the outcomes)

Infants that may not be good candidates for INSURE

- Intubated at birth for apnoeas/poor respiratory effort, unless strong respiratory efforts established after appropriate resuscitation
- Neonates who have received extensive resuscitation
- Any associated medical issues e.g. Anaemia, Hydrops

Procedure

- No premedication.
- [Intubation](#) as per Neonatal Clinical Guidelines.
- Tube size according to the gestational age and weight or a smaller sized ETT.
- Check tube placement with CO₂ indicator, and auscultation.
- Curosurf/ Survanta to be administered in 2 bolus aliquots as per [Surfactant Administration](#) Procedure above.
- Extubate to nCPAP following re-establishment of airflow.
- Establish transcutaneous monitoring to facilitate early and continuous assessment of tolerance of nasal CPAP (should be in place prior to procedure unless INSURE performed in delivery suite).

Before Extubation ensure

- HR & saturations are stable.
- FiO₂ less than the pre-surfactant level.
- No apnoeas.
- Adequate airflow without clinical evidence of airway obstruction
- Nasal CPAP prongs are in position to ensure smooth transfer from ETT CPAP to nasal CPAP and minimise risk of lung collapse

Other recommendations

- One-to-one nursing is recommended for the duration of the administration and observations.
- Senior Registrar or Consultant to supervise administration of appropriate dose of surfactant.

- Ventilate using the Neopuff until stable, transitioning to breathing with Neopuff CPAP support as soon as possible. Use volume monitoring if available.
- If transient bradycardia or desaturation present, briefly stop the dosing procedure and initiate Neopuff.
- Once the infant has stabilized, resume the dosing procedure.
- Keep ventilator as a standby.
- Extubate to nCPAP as soon as possible.
- If possible Registrar/SR to remain on NICU for 30 minutes following extubation.
- Confirm accuracy of T_{cp}CO₂ with a blood gas at ~ 30 minutes after administration to facilitate early recognition of over- or under-ventilation.

Further Reading

Surfactant therapy in neonates

Summary

Surfactant needs to be administered to neonates ventilated for hyaline membrane disease (HMD) and meconium aspiration syndrome. Surfactant therapy may be considered in neonates with pulmonary haemorrhage and severe RSV bronchiolitis. There is no evidence to support the use of surfactant therapy in congenital diaphragmatic hernia. For all indications, most cost-effective and hence preferred surfactant preparation, except in extremely preterm infants (< 25 weeks GA) where Curosurf is to be used. Clinicians may choose to use Curosurf on an individual case basis if they consider that the baby's clinical condition warrants it. Please refer to the NICU drug manual for details of the dose and method of administration of surfactant.

Indications for surfactant therapy in neonates:

Hyaline Membrane Disease

Systematic reviews of multiple RCTs show that animal derived surfactants improve the outcomes of preterm infants with respiratory distress syndrome (Singh, Halliday et al. 2015). Prophylactic surfactant may be of benefit when the infant requires intubation for stabilisation (Rojas-Reyes, Morley et al. 2012, Sweet, Carnielli et al. 2017). The attending neonatologist or the senior registrar will decide regarding whether to administer it prophylactically in the delivery room or later in the NICU. More mature infants who can be stabilised on CPAP.

Pulmonary haemorrhage

A few small observational studies show beneficial effects of surfactant administration in pulmonary haemorrhage. However, no RCTs have examined this issue. Review articles by Aziz (Aziz and Ohlsson 2012), Jasani (Jasani, Kabra et al. 2016) and Keiser (Keiser and Bhandari 2016) conclude that there remains insufficient evidence to recommend the routine use of surfactant after pulmonary haemorrhage in preterm infants.

In an RCT, Bozdog et al (Bozdog, Dilli et al. 2015) compared poractant alfa (n=21) and beractant (n=21) for the treatment of pulmonary haemorrhage in very low birth weight infants. The mean (SD) birth-weight and gestational age were similar for both groups (p = 0.33 and 0.89, respectively). Surfactant preparation had no effect on the oxygenation index (OI) at any time point (p > 0.05). The prevalence of Bronchopulmonary Dysplasia (BPD) and mortality related to pulmonary haemorrhage were similar in both the groups. They concluded that both natural surfactants improved oxygenation when administered for pulmonary haemorrhage in VLBW infants. They also concluded that the type of surfactant seems to have no effect on BPD and

mortality rates in the presence of pulmonary haemorrhage. However, the study is likely underpowered to detect a difference between surfactant preparations given low study numbers.

Meconium aspiration syndrome

The Cochrane review (El Shahed, Dargaville et al. 2014) included four randomised controlled trials that met inclusion criteria. Three out of those four trials used Beractant, whereas one used Poractant. The meta-analysis of four trials (326 infants) showed no statistically significant effect on mortality [(RR) 0.98, 95 % confidence interval (CI) 0.41 to 2.39]. A meta-analysis of two trials (n = 208) using Beractant showed that surfactant administration significantly reduced the risk of requiring extracorporeal membrane oxygenation; [RR 0.64, 95% CI 0.46 to 0.91].

Congenital diaphragmatic hernia

Keiser et al (Keiser and Bhandari 2016) conclude that there remains insufficient evidence to recommend the routine use of surfactant in the management of term infants with CDH, regardless of need for ECMO support. This conclusion includes the subpopulation of preterm infants with CDH. Similar conclusions were drawn by Jasani et al (2016).

Critically ill infants with RSV Bronchiolitis

Jat and Chawla (Jat and Chawla 2015) evaluated the role of surfactant administration in critically ill infants with RSV Bronchiolitis. They identified only three RCTs (total sample size 79) and found that the use of surfactant reduced duration of mechanical ventilation, duration of ICU stay, oxygenation, and improved CO₂ elimination. Two of the included trials used Poractant whereas the other trial used Beractant.

Poractant versus Beractant in preterm infants with RDS

The Cochrane review (Singh, Halliday et al. 2015) identified nine studies that compared modified bovine minced lung surfactant extract (Beractant/Survanta) to porcine minced lung surfactant extract (Poractant/Curosurf) for treatment of respiratory distress syndrome. Meta-analysis of these trials demonstrated a significant increase in the risk of worse outcomes for Beractant: Mortality prior to hospital discharge (RR 1.44, 95 % CI 1.04 to 2.00; 9 studies and 901 infants; moderate quality evidence), death or oxygen requirement at 36 w postmenstrual age (RR 1.30, 95% CI 1.04 to 1.64; 3 studies and 448 infants; moderate quality evidence), and patent ductus arteriosus (PDA) requiring treatment (RR 1.86, 95% CI 1.28 to 2.70; 3 studies and 137 infants).

While at the outset it appears that Curosurf is superior to Survanta, it is important to note that the total sample size was only 901 infants from 9 RCTs. In the same Cochrane review, under the title 'implications for practice', the authors stated that 'caution should be used in the interpretation of this result because of the imprecision in analysis from the small sample size of the studies'. Further, they highlight the uncertainty regarding whether the "observed differences are from differences in dose or from source of extraction (porcine vs. bovine) because of the lack of dose-equivalent comparison groups with appropriate sample size". They also stated that "due to the lack of information about long-term neurodevelopment, respiratory and other health effects, no conclusions can be drawn about the superiority or inferiority of one animal-derived surfactant over another with respect to long-term outcomes".

The European consensus guidelines recommend the use of Poractant for RDS in preterm infants requiring surfactant for increased work of breathing and inspired oxygen requirement (Sweet, Carnielli et al. 2017). Poractant Alfa in an initial dose of 200 mg/kg is better than beractant (initial dose of 100 mg/kg) or 100 mg/kg poractant alfa for rescue therapy but it remains unclear if this difference is due to a dose effect or

differences in the surfactant preparation. The American Academy of Pediatrics (Polin, Carlo et al. 2014) does not make such recommendations. They say it is unclear whether significant differences in clinical outcomes exist among the available animal-derived products.

We published a retrospective cohort study comparing the outcomes of inborn preterm infants <32 w gestation (23-31⁶ between 2005 and 2007. 415 preterm infants (<32 w GA) received surfactant (Curosurf: 214; Survanta: 201) (Paul, Rao et al. 2013). Infants in the Curosurf group were 2.8 days younger than Survanta (27.0 ± 2.3 w PMA vs. 27.4 ± 2.3 w PMA; P = 0.03). All other baseline characters including Clinical Risk Index for Babies II scores were similar for both groups. No significant differences between Curosurf and Survanta were found for the following outcomes: death or chronic lung disease (78/212 vs. 59/200; P = 0.28); death (24/214 vs. 15/201, P = 0.24); moderate to severe chronic lung disease (63/212 vs. 46/200; P = 0.45) and moderate to severe disability (20/163 vs. 19/151, P = 0.98). Subgroup analysis of infants <28 w GA and ≥28 w GA also did not show significant differences between the two types of surfactant. Subgroup analysis of infants <25 w GA showed that Survanta group had higher incidence of the composite outcome of death or CLD (31/40 vs 26/27). Infants >25 w GA who received Curosurf had higher incidence of 'death or CLD' (47/172, 27.3% vs 33/173, 19.3%, p=0.023) (Paul et al, PAS abstract 2012). The results remained the same after multivariate logistic regression analysis. We concluded that until additional high-grade RCT based evidence emerges to support one or other preparation, the results of our local study do not support the need for preferential use of Curosurf or Survanta within our intensive care unit.

Cost of Curosurf versus Survanta for the NCCU of KEMH/PMH:

For our unit, the cost of a 3-mL vial (240 mg surfactant) of Curosurf is \$819, whereas the cost of 8 mL (200 mg surfactant) Survanta is \$346. For a baby with birth weight of 1000 g, the cost of Curosurf using the standard regimen of initial 200 mg/kg (2.5 mL/kg) followed by 100 mg/kg (1.25 mL/kg) is \$1 023 . For a baby with same birth weight, the cost of Survanta using the standard regime of initial dose of 100 mg/kg (4 mL/kg) and subsequent dose of 100 mg/kg (4 mL/kg) is \$ 346 /kg. This represents 2.95 times higher cost for Curosurf over Survanta. Even if one were to use the INSURE technique (intubation, surfactant and extubation) with Curosurf and use only one dose, the cost will be AUD \$682, which is 1.97 times more expensive than two dose regimen of Survanta. Given that Curosurf is very expensive and there is lack of strong evidence of long-term benefit, our preference is to use Survanta in the NCCU for all indications except in extremely preterm infants (≤25 weeks) where Curosurf is to be used. Clinicians may choose to use Curosurf on an individual case basis if they consider that the baby's clinical condition warrants it.

INSURE Method

Background

Respiratory Distress Syndrome is the most important cause of mortality and morbidity in preterm infants. The optimal approach to surfactant treatment is still being refined, more than 60 years after its discovery. Introduction of CPAP more than halved the mortality from 55 % to 20 % and surfactant treatment has halved the mortality from 20 % to 10 %.

Evidence from systematic reviews show that early surfactant treatment reduces mortality and decreases the incidence of chronic lung disease (CLD) and air leaks in

preterm infants at risk of RDS (Yost and Soll 2000). Multiple reviews since then have shown the benefit of early surfactant use.

One of the major drawbacks of the conventional approach to surfactant administration are the complications and adverse effects associated with continuation of mechanical ventilation including inflammatory lung injury that may increase the risk of other complications associated with prolonged need for mechanical ventilatory support including adverse neurodevelopmental outcomes, subglottic stenosis/ cyst formation (Johnson, Rutter et al. 2005), and voice changes (French, Kelly et al. 2013).

Why INSURE?

Increasingly, non-invasive respiratory support is achieved through nasal continuous positive airway pressure (CPAP). Nasal CPAP is associated with a decreased risk of developing chronic lung disease compared with conventional mechanical ventilation. An INTubate, SURfactant, and Extubation (INSURE) strategy has been successfully applied both early and late in the course of respiratory distress syndrome. While we are waiting for more evidence for administering exogenous surfactant through non-invasive approaches this INSURE seems to be the most reasonable method of administering surfactant in the eligible and suitable group of infants (Pfister and Soll 2012). Meta-analysis of nasal CPAP with/without INSURE are currently underpowered, however appear to favour early INSURE over nCPAP alone for reducing BPD, BPD or death and air leak (Isayama, Chai-Adisaksopha et al. 2015).

Current Evidence for INSURE

The INSURE method has been reported in several different contexts and compared with existing respiratory support strategies. Both early INSURE (during initial hour of life) and late INSURE (used later in the course of established RDS) strategies have been compared with the conventional standard approach of intubation, surfactant administration and continued mechanical ventilation and compared with continued nasal CPAP.

The INSURE method seems to reliably reduce the burden of mechanical ventilation in preterm infants with RDS with early INSURE being more beneficial. Some infants still fail, requiring re-intubation and mechanical ventilation (30-50%) (Pfister and Soll 2012)

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Related WNHS policies, procedures and guidelines

Neonatal Clinical Guideline - [Intubation](#)

[Neonatal Medication Protocols](#) – [Survanta](#)

[Curosurf](#)

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