ALBUMIN 4%
NEWBORN USE ONLY

2019

Alert	Albumex® 4 is normally clear or slightly opalescent. If it appears to be turbid, it must not be used and the bottle should be returned unopened to the Australian Red Cross Blood Service. Albumin is not recommended as the initial resuscitating fluid in hypotensive infants. If the product has been stored in the refrigerator it should be allowed to reach room temperature before administration.
Indication	Hypovolaemia/shock with or without hypoalbuminaemia Plasma exchange [normal saline recommended]
Action	Albumin is involved in the maintenance of colloid osmotic pressure, binding and transport of plasma compounds (bilirubin, bile acids, long-chain fatty acids, thyroxine, vitamin D, calcium, magnesium, copper, zinc), renders some potential toxins harmless, is a carrier of nitric oxide and affects pharmacokinetics of many drugs. Albumin 4% is approximately isotonic with osmolality 260 mOsm/kg and pH 6.7 to 7.3. The half-life of albumin is about 19 days.
Drug Type	Plasma product, manufactured from human plasma collected by the Australian Red Cross Blood Service.
Trade Name	Albumex® 4
Presentation	Albumex® 4 50 mL (2 g albumin), 250 mL (10 g albumin) and 500 mL (20 g albumin) bottles. Each bottle contains Human Albumin 40 g/L, sodium 140 mmol/L, chloride 128 mmol/L and octanoate 6.4 mmol/L. Albumex® 4 contains trace amounts of aluminium (≤200 microg/L).
Dosage/Interval	Hypovolaemia/shock 10 to 20 mL/kg over 10 to 60 minutes titrated to clinical response. Plasma exchange [normal saline recommended]: $Volume\ albumin\ 4\%\ (mL) = total\ blood\ volume\ x\ \frac{(observed\ PCV - desired\ PCV)}{observed\ PCV}$ Where total blood volume = 80 mL/kg; desired PCV = 0.55 Infusion rate to match 1:1 with the rate of removal of blood.
Maximum daily dose	
Route	Intravenous
Preparation/Dilution	Administer undiluted 1. If the product has been stored in the refrigerator it should be allowed to reach room temperature before administration. 2. Always record the name and batch number of the product in order to maintain a link between the patient and the batch of the product. <u>Dilution of Albumex® 20 to Albumin 4% in case of unavailability of albumin 4%</u> Albumex® 20 can be diluted to an iso-oncotic protein concentration (4 to 5% albumin) prior to administration. Dilute in the proportion of 1 mL of Albumex® 20 to 4 mL of crystalloid solution (sodium chloride 0.9% or glucose 5% or 10%). DO NOT dilute with water since the lower tonicity will lead to intravascular haemolysis.
Administration	Intravenously over 10 to 60 minutes titrated to clinical response. Albumex® 4 is packaged in a glass bottle that must be vented during use. [1]
Monitoring	Continuous cardiorespiratory and temperature observations.
Contraindications	History of allergy to albumin.
Precautions	Cardiac failure, pulmonary oedema or severe anaemia. The sodium concentration in this product is 140 mmol/L. This should be noted when the product is used in patients requiring sodium restriction. Administration of albumin can aggravate myocardial depression in patients with shock.
Drug Interactions	Hypotension has been reported in patients given albumin who are on angiotensin converting enzyme (ACE) inhibitors. The addition of other medicines to Albumex® 4 has not been evaluated.
Adverse Reactions	Allergic reactions. Possible harms associated with albumin infusion in neonates include fluid overload (pulmonary oedema, impaired gas exchange, worsening oxygenation, chronic lung disease, patent ductus arteriosus, myocardial dysfunction especially for infants with birth asphyxia), neurological injury

	(cerebral oedema, intraventricular haemorrhage due to rapid bolus administration), salt loading and fluid retention.
Compatibility	Glucose 5% and 10%, glucose-sodium chloride combination. [2]
Incompatibility	Albumex® 4 should not be mixed with protein hydrolysates, amino acid solutions, solutions containing alcohol or solutions containing drugs that bind to albumin (e.g. calcium channel blockers, antibiotics and benzodiazepines).
Stability	
Storage	Store below 30°C (Do not freeze). Protect from light. If the product has been stored in the refrigerator it should be allowed to reach room temperature before administration. Do not use if the solution has been frozen.
Special Comments	
Evidence summary	**Efficacy** **Hypotensive preterm infants:** Two RCTs [3, 4] have compared volume expansion using albumin 5% to normal saline 10 mL/kg in hypotensive preterm infants. Meta-analysis [5] found no significant difference in mortality (typical RR 1.02; 95% CI 0.50, 2.06) or PIVH. No data were available for periventricular leukomalacia (PVL) or long-term disability. Meta-analysis found no significant difference in treatment failure (2 studies, 163 infants; typical RR 0.76, 95% CI 0.54, 1.07) although there was substantial heterogeneity between studies. There were no significant differences for other neonatal morbidities including BPD, PDA, NEC and sepsis. One trial [6] with 20 infants in each group with a systolic BP <40 mmHg compared fresh frozen plasma to albumin 4.5% 15 mL/kg and reported no difference in change in mean BP, although both these groups had a significantly greater increase in mean BP than a control group who received albumin 20% 5 mL/kg. Other outcomes were not reported. Systematic review concluded there is insufficient evidence to determine whether infants with cardiovascular compromise benefit from volume expansion or what type of volume expansion should be used in preterm infants (if at all) [5]. In addition, two RCTs [7, 8] have compared albumin 4.5% 15 to 20 mL/kg to dopamine in a total of 63 hypotensive preterm infants. Systematic review [9] found dopamine was more successful than albumin at correcting low BP in hypotensive preterm infants, but neither dopamine nor albumin improved blood flow, mortality or morbidity in preterm infants. A systematic review of RCTs comparing albumin or PPF with no albumin or PPF or with a crystalloid solution in critically ill patients with hypovolaemia, burns or hypoalbuminaemia included 38 trials with 1,958 deaths among 10,842 participants [10]. Several trials were in newborn infants although no subgroup analysis was performed. Overall, for hypovolaemia there was no difference in death following albumin administration (RR 1.02, 95% CI 0.92 to 1.13). For burns, the relative risk was 2.93 (95% CI 1.28 to 6.72) and for hypoalbuminaemia the relative risk was 1.26 (95% CI 0.84 to 1.88). Conclusion: Albumin solutions cannot be recommended as treatment for hypotension in newborn infants. [LOE I, GOR C] **Hyperbilirubinaemia:** Trials of albumin infusion pre-exchange transfusion for severe neonatal jaundice reported use of albumin 20% (see albumin 20% formulary). **Polycythaemia:** A single RCT [11] compared isotonic saline versus 5% albumin in 102 term infants as replacement fluid in partial exchange transfusion (PET) for the treatment of neonatal polycythaemia. PET with either resulted in a decline in haematocrit up to 24 hours after PET with no difference between groups and no adverse event reported. A systematic review [12] of PET for polycythaemia, most RCTs compared plasma preparations to no treatment. The review reported there are no proven clinically significant short or long-term benefits of PET in polycythaemic newborn infants who are clinically well or who have minor symptoms related to hyperviscosity, and there may be an increased risk of NEC. Conclusion: Albumin solutions cannot be recommended as the preferred method of PET for polycythaemia. [LOE II GOR C]

	Liver cirrhosis and nephrotic syndrome: Hypoalbuminemia, oedema and ascites may be manifestation of liver cirrhosis and nephrotic syndrome [13]. ***Liver disorders:*** No studies have reported on the use of albumin infusion therapy in neonates with liver disorders. Infusions of albumin has been used in infants and children undergoing high volume paracentesis with a reported lower incidence of post-paracentesis circulatory dysfunction and asymptomatic hyponatremia but no difference in other clinical outcome [14]. However, as a fluid extraction of <200 mL/kg at a slow rate was associated with better haemodynamic stability, albumin infusion is not recommended [13, 14]. ***Nephrotic syndrome:*** In infants with congenital nephrotic syndrome and massive oedema, treatment with intravenous albumin and diuretic infusions has been used. However, the treatment has a risk of respiratory failure and congestive heart failure, so use of albumin infusion is cautioned [13]. **Safety** There are insufficient data from RCTs in newborn infants to determine the safety of albumin infusion for any indication, although no adverse events attributable to albumin infusion were reported in trials in newborn infants [5, 9, 15]. Human albumin contains no preservatives and undergoes a rigorous pasteurisation process to ensure pathogen inactivation. It does not contain isoagglutinins or blood group substances; hence the risk of minor or major incompatibility is impossible. Additionally, hypersensitivity reactions such as flushing, urticaria, fever and nausea rarely occur following its administration, since albumin preparations are considered non-immunogenic [13]. However, possible harms associated with albumin infusion in neonates include fluid overload (pulmonary oedema, impaired gas exchange, worsening oxygenation, chronic lung disease, patent ductus arteriosus, myocardial dysfunction especially for infants with birth asphyxia), neurological injury (cerebral oedema, intraventricular haemorrhage due to rapid bolus administration), salt loading and fluid retention, and higher cost compared with crystalloids [13].
References	1. MIMS online. Accessed on 18 July 2019. 2. Australian Injectable Drugs Handbook, 7th Edition, Society of Hospital Pharmacists of Australia. 2019. 3. Lynch SK, Mullett MD, Graeber JE, Polak MJ. A comparison of albumin-bolus therapy versus normal saline-bolus therapy for hypotension in neonates. J Perinatol. 2008;28:29-33. 4. So KW, Fok TF, Ng PC, Wong WW, Cheung KL. Randomised controlled trial of colloid or crystalloid in hypotensive preterm infants. Arch Dis Child Fetal Neonatal Ed. 1997;76:F43-6. 5. Osborn DA, Evans NJ. Early volume expansion for prevention of morbidity and mortality in very preterm infants. Cochrane Database of Systematic Reviews. 2004. 6. Emery EF, Greenough A, Gamsu HR. Randomised controlled trial of colloid infusions in hypotensive preterm infants. Arch Dis Child. 1992;67:1185-8. 7. Gill AB, Weindling AM. Randomised controlled trial of plasma protein fraction versus dopamine in hypotensive very low birthweight infants. Arch Dis Child. 1993;69:284-7. 8. Lundstrom K, Pryds O, Greisen G. The haemodynamic effects of dopamine and volume expansion in sick preterm infants. Early Hum Dev. 2000;57:157-63. 9. Osborn DA, Evans NJ. Early volume expansion versus inotrope for prevention of morbidity and mortality in very preterm infants. Cochrane Database of Systematic Reviews. 2001. 10. Roberts I, Blackhall K, Alderson P, Bunn F, Schierhout G. Human albumin solution for resuscitation and volume expansion in critically ill patients. Cochrane Database of Systematic Reviews. 2011. 11. Wong W, Fok TF, Lee CH, Ng PC, So KW, Ou Y, Cheung KL. Randomised controlled trial: comparison of colloid or crystalloid for partial exchange transfusion for treatment of neonatal polycythaemia. Arch Dis Child Fetal Neonatal Ed. 1997;77:F115-8. 12. Ozek E, Soll R, Schimmel MS. Partial exchange transfusion to prevent neurodevelopmental disability in infants with polycythemia. Cochrane Database Syst Rev. 2010:CD005089. 13. Shalish W, Olivier F, Aly H, Sant'Anna G. Uses and misuses of albumin during resuscitation and in the neonatal intensive care unit. Seminars in Fetal and Neonatal Medicine. 2017;22:328-35.

	14. Church JT, Antunez AG, Dean A, Matusko N, Deatrick KB, Attar MA, Gadepalli SK. Evidence-based management of chylothorax in infants. Journal of Pediatric Surgery. 2017;52:907-12. 15. Jardine LA, Jenkins-Marsh S, Davies MW. Albumin infusion for low serum albumin in preterm newborn infants. Cochrane Database of Systematic Reviews. 2004.

Original version Date: 22/07/2019	**Author: ANMF Group**
Current Version number: 1.0	**Current Version Date: 22/07/2019**
Risk Rating: Medium	**Due for Review:** 22/07/2024

Authors Contribution

Original author/s	Srinivas Bolisetty
Evidence Review	David Osborn
Nursing Review	Eszter Jozsa
Pharmacy Review	Jing Xiao, Michelle Jenkins
ANMF Group contributors	Nilkant Phad, Himanshu Popat, James Marceau
Final content and editing review of the original	Ian Whyte
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty