ALBUMIN 20%
NEWBORN USE ONLY

2024

Alert	Albumex® 20 and Alburex® 20 products are normally clear or slightly opalescent. Due to differences in the manufacturing processes albumin products can vary in colour; it is a clear, almost colourless, yellow, amber, or green liquid. If it appears turbid it must not be used, and the bottle should be returned unopened to the Australian Red Cross Lifeblood.[16] **Albumin 20% must not be used 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.[16] From late 2023, Albumex® 20 has been discontinued and replaced by Alburex® 20 AU. The transition is expected to be completed in 2025.
Indication	Hypoalbuminaemia
Action	Albumin is involved in the maintenance of colloid osmotic pressure, binding, and transport of plasma compounds (bilirubin, bile acids, long-chain fatty acids, thyroxin, vitamin D, calcium, magnesium, copper, zinc), renders some potential toxins harmless, is a carrier of nitric oxide, and affects pharmacokinetics of many drugs. The half-life of albumin is about 19 days.
Drug Type	Plasma product, manufactured from human plasma collected in Australia by the Australian Red Cross Lifeblood.
Trade Name	Albumex® 20 (being discontinued in Australia), Alburex® 20 AU
Presentation	**Albumex® 20:** 10 mL (2 g albumin) and 100 mL (20 g albumin) glass bottles. Each bottle of Albumex® 20 contains human albumin 200 g/L and sodium 48 to 100 mmol/L. Albumex® 20 contains trace amounts of aluminium (≤200 microgram/L). Osmolality is 130 mOsm/kg. **Alburex® 20:** 50mL (10g albumin) and 100mL (20g albumin) glass bottles. Each bottle of Alburex® 20 contains human albumin 200 g/L and sodium 140 mmol/L. Osmolality is 258 mOsm/kg (closer to osmolality of human serum in comparison to Albumex® 20).
Dose	IV 0.5 to 1 g/kg/dose (2.5 to 5 mL/kg/dose) of albumin 20%.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – Risk of circulatory overload. Hepatic impairment – No information.
Maximum daily dose	No information.
Route	Intravenous infusion over 2 to 4 hours.
Preparation	Administer undiluted. • If the product has been stored in the refrigerator, it should be allowed to reach room temperature before administration. • Always record the name and batch number of the product to maintain a link between the patient and the batch of the product. • Alburex® 20 AU is packaged in a glass bottle that must be vented during use. [18] <u>Dilution of albumin 20% to albumin 5% in case of unavailability of albumin 5%</u>[16, 18] Albumin 20% can be diluted to an iso-oncotic protein concentration (5% albumin) prior to administration. To make albumin 5%: For each 1 mL of Albumin 20%, add 3 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	Intravenous infusion over 2 to 4 hours. Glass bottle must be vented during administration.
Monitoring	Continuous cardiorespiratory and temperature observations. Electrolytes[18].
Contraindications	Known hypersensitivity to albumin preparations or to any of the excipients.
Precautions	Cardiac failure, pulmonary oedema, or severe anaemia. The sodium concentration in this product varies from 48 to 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.
Adverse Reactions	Mild reactions (e.g. flush, urticaria, fever, and nausea) – Rare. These reactions normally disappear rapidly when the infusion rate is slowed down, or the infusion is stopped. Hypotension, chills, fever. Allergic reactions. Circulatory overload. Neurological injury (cerebral oedema, intraventricular haemorrhage due to rapid bolus administration). Salt loading and fluid retention. Aluminium - Albumex® 20 contains trace amounts of aluminium (≤200 microgram/L). Accumulation of aluminium in adult patients with chronic renal insufficiency has led to toxic manifestations such as hypercalcaemia, vitamin D-refractory osteodystrophy, anaemia, and severe progressive encephalopathy.[16]
Overdose	Manage circulatory overload. For further information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).
Compatibility	Fluids:[17] Glucose 5% and 10%, glucose-sodium chloride combination, sodium chloride 0.9%, and sodium chloride 0.45%. Y-site:[17] Cloxacillin, diltiazem, esmolol, hydrocortisone, ketamine, lorazepam, meropenem, and metoprolol.
Incompatibility	Fluids:[17] Amino acid solutions (extrapolated from 3 in 1 TPN solution result) Y-site:[17] Fat emulsion, fosfomycin, labetalol, meropenem/vaborbactam, micafungin, midazolam, plazomicin, vancomycin, and verapamil.
Stability	Albumin preparations must be used immediately after opening the bottle. Discard any unused solution. Use in one patient on one occasion only. Do not use if the solution has been frozen.
Storage	Protect from light. **Albumex® 20** 10 mL: Store at 2°C to 8°C (Refrigerate. Do not freeze). 100 mL: Store below 30°C (Do not freeze). **Alburex® 20 AU** Store below 25°C (do not freeze).
Excipients	**Albumex® 20:** Sodium (48-100 mmol/L), octanoate 32 mmol/L, and water for injections.[16] **Alburex® 20 AU:** Sodium acetyltryptophanate 16 mmol/L, sodium octanoate 16 mmol/L, sodium chloride (added to meet required sodium content), and water for injections.[18]
Special Comments	
Evidence	**Efficacy** **Hypoalbuminemia:** Two randomised, controlled trials (RCT)[1,2] have compared 5 mL/kg albumin 20% (1 g/kg) infusion in preterm infants with plasma albumin <30 g/L. One study[1] did not report major clinical outcomes. The other study[2] reported no difference in mortality, peri/intraventricular haemorrhage (PIVH), patent ductus arteriosus (PDA), necrotising enterocolitis (NEC), bronchopulmonary dysplasia (BPD), and duration of mechanical ventilation and oxygen therapy. Systematic review concluded there is a lack of evidence from randomised trials to determine whether the routine use of albumin infusion in preterm neonates with low serum albumin reduces mortality or morbidity, and no evidence to assess whether albumin infusion is associated with significant side effects.[3] A systematic review of RCTs comparing albumin or plasma protein fraction (PPF) with no albumin or PPF or with a crystalloid solution in critically ill patients with hypoalbuminaemia included 12 trials with 121 deaths among 757 participants.[4] Several trials were in newborn infants although no subgroup analysis was performed. The review found insufficient evidence to determine the efficacy and safety of albumin 20% infusion in newborn infants with hypoalbuminaemia. [LOE II GOR D] Recommendation was for albumin infusion to only be considered in neonates with overwhelming

continuous albumin loss including significant chylothorax, high-output ostomy drainage, and severe congenital nephrotic syndrome.[5]

Chylothorax: Although chyle contains 22.4 g/L (12.6 to 30 g/L) of albumin, there are no studies of albumin replacement in high output chylothorax, and recent reviews on chylothorax management have not recommended albumin infusion.[5,6]

Liver cirrhosis and nephrotic syndrome: Hypoalbuminemia, oedema, and ascites may be manifestation of liver cirrhosis and nephrotic syndrome.[5] ***Liver disorders:*** No studies reported on the use of albumin infusion therapy in neonates with liver disorders. 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.[7] However, as a fluid extraction of <200 mL/kg at a slow rate was associated with better haemodynamic stability, albumin infusion is not recommended.[6,7] ***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.[6]

Hypotensive preterm infants: One trial[8] 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% 5mL/kg. Other outcomes were not reported.

Conclusion: Albumin 20% solution cannot be recommended as treatment of hypotension in newborn infants. [LOE II, GOR C]

Routine treatment of preterm infants: One study[9] randomised 25 normotensive preterm infants to routine treatment with albumin 20% 15 mL/kg (3 g/kg) or no treatment and reported no difference in mortality (RR 0.92, 95% CI 0.23, 3.72) or periventricular leukomalacia. Conclusion: Albumin 20% solution cannot be recommended as routine treatment in preterm infants. [LOE I GOR C]

Hyperbilirubinaemia: Trials of albumin infusion pre-exchange transfusion for severe neonatal jaundice have reported heterogeneous results. Chan et al[10] compared albumin 1 g/kg versus no treatment pre-exchange in 42 infants with severe neonatal jaundice and reported no difference in albumin-binding capacity, bilirubin, albumin, or red cell bilirubin at pre- and one-hour post-albumin infusion in the primed infants. All infants received an exchange transfusion. Shahian et al[11] in 50 infants with severe jaundice compared 5 mL/kg of albumin 20% (1 g/kg) to no treatment pre-exchange transfusion. Bilirubin concentration was lower than at 6 and 12 hours post-exchange (P<0.001), duration of phototherapy was reduced (8.6 vs. 25 hours; P<0.001) and none of 25 needed repeat exchange transfusion compared to 4/25 in the control group.

Dash et al[12] compared 5 mL/kg of 20% human albumin (n=23) versus saline (n=27) infusion one hour prior to exchange transfusion. Phototherapy duration was not different [Median 29 vs. 33 hours; P=0.76], serial changes in total serum bilirubin following exchange transfusion and need for repeat exchange transfusion were similar (2/23 versus 2/27).

A systematic review[13] compared IV fluid supplementation versus no fluid supplementation in newborn infants with unconjugated hyperbilirubinaemia who required phototherapy. Duration of phototherapy was significantly shorter for fluid-supplemented infants, (MD −10.70 hours, 95%CI −15.55 to −5.85; participants = 218; studies = 3; I^2 = 67%) and fluid-supplemented infants were less likely to require exchange transfusion (RR 0.39, 95% CI 0.21 to 0.71; participants = 462; studies = 6; I^2 = 72%). There was no evidence that IV fluid supplementation affected important clinical outcomes such as bilirubin encephalopathy, kernicterus, or cerebral palsy.

Conclusion: Heterogeneous evidence suggests intravenous fluid treatment may reduce serum bilirubin levels and exchange transfusion requirements in infants with unconjugated hyperbilirubinaemia, although there is no evidence of a reduction in bilirubin encephalopathy, kernicterus, or cerebral palsy.[11,13] [LOE I GOR C] There is no evidence that albumin solutions are more efficacious than saline for reducing bilirubin or repeat exchange transfusion in infants undergoing exchange transfusion for hyperbilirubinaemia.[12] [LOE II GOR C]

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[3,14,15] 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.[5] 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, and myocardial dysfunction especially for infants with birth asphyxia), neurological injury (cerebral oedema, and intraventricular haemorrhage due to rapid bolus administration), salt loading and fluid retention, and higher cost compared with crystalloids.[5] **Pharmacokinetics** In healthy subjects, less than 10% of infused albumin leaves the intravascular compartment during the first 2 hours following infusion. In some patients the plasma volume can remain increased for some hours. However, in critically ill patients, albumin can leak out of the vascular space in substantial amounts at an unpredictable rate.[16]
Practice points	
References	1. Greenough A, Emery E, Hird MF, Gamsu HR. Randomised controlled trial of albumin infusion in ill preterm infants. Eur J Pediatr. 1993;152:157-9. 2. Kanarek KS, Williams PR, Blair C. Concurrent administration of albumin with total parenteral nutrition in sick newborn infants. JPEN J Parenter Enteral Nutr. 1992;16:49-53. 3. Jardine LA, Jenkins-Marsh S, Davies MW. Albumin infusion for low serum albumin in preterm newborn infants. Cochrane Database of Systematic Reviews. 2004. 4. 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. 5. 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. 6. 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. 7. Sen Sarma M, Yachha SK, Bhatia V, Srivastava A, Poddar U. Safety, complications and outcome of large volume paracentesis with or without albumin therapy in children with severe ascites due to liver disease. Journal of Hepatology. 2015;63:1126-32. 8. Emery EF, Greenough A, Gamsu HR. Randomised controlled trial of colloid infusions in hypotensive preterm infants. Arch Dis Child. 1992;67:1185-8. 9. 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. 10. Chan G, Schiff D. Variance in albumin loading in exchange transfusions. J Pediatr. 1976;88:609-13. 11. Shahian M, Moslehi MA. Effect of albumin administration prior to exchange transfusion in term neonates with hyperbilirubinemia--a randomized controlled trial. Indian Pediatr. 2010;47:241-4. 12. Dash N, Kumar P, Sundaram V, Attri SV. Pre exchange Albumin Administration in Neonates with Hyperbilirubinemia: A Randomized Controlled Trial. Indian Pediatr. 2015;52:763-7. 13. Lai NM, Ahmad Kamar A, Choo YM, Kong JY, Ngim CF. Fluid supplementation for neonatal unconjugated hyperbilirubinaemia. Cochrane Database of Systematic Reviews. 2017;8:CD011891. 14. 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. 15. Osborn DA, Evans NJ. Early volume expansion for prevention of morbidity and mortality in very preterm infants. Cochrane Database of Systematic Reviews. 2004. 16. Albumex® 20 Product Information. https://www.cslbehring.com.au/-/media/cslb-australia/documents/aus-pis-and-cmis/albumex-20-au-pi-1300.pdf. Obtained on 31 July 2024. 17. MerativeTM Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: July/31/2024).

	18. Alburex® 20 AU Product information. https://labeling.cslbehring.com/PI/AU/Alburex/EN/Alburex-20-AU-Product-Information.pdf Obtained on 1 August 2024

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