

Alert	Albumex® 20 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 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.
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. Albumin 20% is hyper-oncotic but hypo-osmotic (130 mOsm/kg) compared to human serum with a 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® 20
Presentation	Albumex® 20 – 10 mL (2 g albumin) and 100 mL (20 g albumin) bottles. Each bottle contains Human Albumin 200 g/L and sodium 48 to 100 mmol/L. Albumex® 20 contains trace amounts of aluminium (≤200 micrograms/L).
Dosage/Interval	IV 0.5 to 1 g/kg/dose (2.5 to 5 mL/kg/dose) of Albumex® 20.
Maximum daily dose	
Route	Intravenous Infusion over 2–4 hours.
Preparation/Dilution	Administer undiluted. <ol style="list-style-type: none"> 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 be recorded in order to maintain a link between the patient and the batch of the product. <p><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.</p>
Administration	Intravenously over 2 to 4 hours. Albumex 20 is packaged in a glass bottle that must be vented during use. ¹⁷
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 varies between 48 and 100 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® 20 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. ¹⁸
Incompatibility	Albumex® 20 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	10 mL: Store at 2°C to 8°C (Refrigerate. Do not freeze). 100 mL: Store below 30°C (Do not freeze). Protect from light.
Special Comments	
Evidence summary	<p>Efficacy</p> <p>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, although one of the studies did not report major clinical outcomes. The other study [2] reported no difference in mortality (RR 1.5, 95% CI 0.3–7.43), peri/intraventricular haemorrhage (PIVH), patent ductus arteriosus (PDA), necrotising enterocolitis (NEC), bronchopulmonary dysplasia (BPD), 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].</p> <p>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. Overall, for hypoalbuminaemia the relative risk for mortality was 1.26 (95% CI 0.84 to 1.88).</p> <p>Conclusion: There is insufficient evidence to determine the efficacy and safety of albumin 20% infusion in newborn infants with hypoalbuminaemia. [LOE II GOR D] Recommendation is 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].</p> <p>Chylothorax: Although chyle contains 22.4 g/L (12.6 to 30) 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].</p> <p>Liver cirrhosis and nephrotic syndrome: Hypoalbuminemia, oedema and ascites may be manifestation of liver cirrhosis and nephrotic syndrome [5]. 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 [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].</p> <p>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]</p> <p>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</p>

	<p>leukomalacia. Conclusion: Albumin 20% solution cannot be recommended as routine treatment in preterm infants. [LOE I GOR C]</p> <p>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.</p> <p>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).</p> <p>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; I² = 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; I² = 72%). There was no evidence that IV fluid supplementation affected important clinical outcomes such as bilirubin encephalopathy, kernicterus or cerebral palsy.</p> <p>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]</p> <p>Safety</p> <p>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, 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 [5].</p>
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