New Zealand Data Sheet

Albumex® 4

Human Albumin 4% (40 g/L)

NAME OF THE MEDICINE

Human albumin, solution for intravenous infusion.

DESCRIPTION

Albumex® 4 is manufactured from human plasma donated by New Zealand's voluntary and non-remunerated donors. Albumex® 4 is a clear, slightly viscous liquid; it is almost colourless, yellow, amber or green. It is prepared by a combination of the Cohn cold-ethanol fractionation process and chromatographic techniques. It is a sterile, preservative free 4% w/v human albumin solution which is iso-oncotic with human serum. It has a nominal osmolality of 260 mOsm/kg, is approximately isotonic and the pH is 6.7 to 7.3. The manufacturing process for Albumex® 4 contains dedicated steps to reduce the possibility of virus transmission including pasteurisation (heating at 60°C for 10 hours) and incubation at low pH to inactivate viruses. The nominal composition of Albumex® 4 is as follows:

Human Albumin	40 g/Litre
Sodium	140 mmol/Litre
Chloride	128 mmol/Litre
Octanoate	6.4 mmol/Litre

PHARMACOLOGY

Albumin accounts quantitatively for more than half of the total protein in the plasma and represents about 10% of the protein synthesis activity of the liver. The metabolic half-life of albumin *in vivo* is about 19 days and the turnover in an adult is approximately 15 g per day. There is rapid interchange of albumin between the intra- and extravascular spaces.

Albumex® 4 is iso-oncotic with human serum. When infused into adequately hydrated patients its effect is to expand the circulating blood volume by an amount approximately equal to the volume of Albumex® 4 infused.

CLINICAL TRIALS

A large multicentre, double blind, randomised controlled trial was conducted to determine the effect of fluid resuscitation with either albumin or saline on mortality in a heterogeneous

population of patients in the ICU. This Saline versus Albumin Fluid Evaluation (SAFE) study was a collaboration of the Australian and New Zealand Intensive Care Society Clinical Trials Group, the Australian Red Cross Blood Service and the George Institute for International Health.

The trial randomised 6997 patients to receive either albumin 4% (Albumex® 4)(n = 3497) or normal (0.9%) saline (n = 3500). The two groups had similar baseline characteristics with randomisation stratified at each centre to ensure each institution enrolled equal numbers of patients for each treatment. Death from any cause during the 28 days after randomisation was the primary outcome measure. There were 726 deaths in the albumin group and 729 deaths in the saline group (relative risk of death 0.99, 95% confidence interval 0.91 to 1.09, p = 0.87).

The proportion of patients with new single or multiple organ failure was similar in the two groups (p = 0.85). There were also no statistically significant differences between the two groups in the secondary outcomes measured: mean (±SD) number of days spent in ICU (6.5±6.6 in the albumin group and 6.2±6.2 in the saline group, p = 0.44), days spent in hospital (15.3±9.6 and 15.6±9.6 respectively, p = 0.30), days of mechanical ventilation (4.5±6.1 and 4.3±5.7, respectively, p = 0.74) or days of renal replacement therapy (0.5±2.3 and 0.4±2.0, respectively, p = 0.41).

This study concluded that in patients in the ICU, use of either 4% albumin or normal (0.9%) saline for fluid resuscitation results in similar mortality at 28 days.

INDICATIONS

Hypovolaemia/shock

Preservation of an adequate circulating blood volume should be the primary aim of therapy. Albumex® 4 may be the initial plasma expander of choice if shock is associated with significant hypoalbuminaemia (albumin concentration less than 25 g/Litre), or if it is clinically desirable to avoid the infusion of large volumes of crystalloid solutions. Albumex® 4 may also be useful following initial resuscitation with crystalloid or synthetic colloid solutions in patients in whom extended support of the intravascular volume is required, such as seriously ill patients with multiple organ failure or the systemic capillary leak syndrome.

Cardiopulmonary bypass

Albumex® 4 may be used for priming the pump for cardiopulmonary bypass surgery for patients with poor left ventricular function, and other complicating factors such as long

bypass time, anaemia or repeat surgery. For post-operative hypovolaemia Albumex® 4 may be used if further colloid is required after a moderate amount of synthetic colloid (1–2 L) has been given or there is ongoing bleeding or anaemia until cross-matched blood is available.

Plasma exchange

Albumex® 4 is indicated as a replacement solution in plasma exchange procedures, particularly when the volume exchanged exceeds 20 mL/kg body weight. In patients with thrombotic thrombocytopenic purpura, fresh frozen plasma may be a preferred replacement.

CONTRAINDICATIONS

Albumex® 4 must not be used if there is a history of allergy to this product. Albumin is contraindicated in patients with cardiac failure, pulmonary oedema or severe anaemia.

PRECAUTIONS

Patients with cardiac failure, renal insufficiency, stabilised chronic anaemia or on cardiopulmonary bypass are at special risk of developing circulatory overload. When being infused with Albumex® 4 they should be carefully monitored for this potential complication.

Two potential risks when using plasma volume expanders are allergic reactions and the risk of circulatory overload. Hypersensitivity is rare when human albumin solution is used because of the human origin of the product, and circulatory overload can be avoided by monitoring the rate and volume of infusion. Should an anaphylactic reaction to Albumex® 4 develop, the infusion should be stopped and treatment instituted with adrenaline, hydrocortisone and antihistamines, as appropriate. Circulatory overload can be avoided by monitoring the rate and volume of infusion. Hypotension and rigors have been associated with human albumin solutions. Administration of albumin can aggravate myocardial depression when present in patients with shock.

No comparative clinical study with Albumex® 4 has been carried out. However such data exists for a similar product, Albumex® 5 which has been compared with 5% NSA in an open apheresis study carried out in five Australian apheresis clinics. Adverse experiences noted in that study are set out below as a guide to users of this product (Albumex® 4).

The rise in blood pressure which may follow rapid administration of albumin necessitates observation of the injured patient to detect bleeding points which failed to bleed at the lower blood pressure; otherwise, new haemorrhage and shock may occur.

The use of albumin for fluid resuscitation of patients with traumatic brain injury is not recommended.

Hypotension: Hypotension has been associated with human albumin solutions. Hypotension following administration of albumin can aggravate myocardial depression when present in patients with shock.

Albumex® 4 contains trace amounts of aluminium (≤200 µg/L). Accumulation of aluminium in patients with chronic renal insufficiency has led to toxic manifestations such as hypercalcaemia, vitamin D-refractory osteodystrophy, anaemia and severe progressive encephalopathy. Therefore, when large volumes of albumin are contemplated for administration to such patients, serious consideration of these potential risks relative to the anticipated benefits should be given.

The addition of other medicines to Albumex® 4 has not been evaluated (See **Compatibility with other fluids**).

Pathogen safety

This product is made from human plasma. Products made from human plasma may contain infectious agents such as viruses and theoretically Creutzfeldt-Jakob Disease (CJD) agents, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain infectious agents and by testing for the presence of certain viral markers.

In addition, virus inactivation/removal procedures are included in the manufacturing process. The current process and procedures applied in the manufacture of this product are effective against enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), and the non-enveloped virus, hepatitis A virus (HAV). These procedures may be of limited value against the non-enveloped virus, parvovirus B19.

Despite these measures, such products may still potentially transmit disease. There is also the possibility that other known or unknown infectious agents may be present in such products.

Vaccination for patients in receipt of medicinal products from human plasma should be considered where appropriate.

Effects on fertility

No studies examining the effect of Albumex® 4 on fertility have been conducted.

Use in pregnancy

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials; therefore, it should be given to pregnant women only if clearly needed.

Use in lactation

No information available.

Paediatric use

There have been no specific clinical studies of Albumex® 4 in children.

Use in the elderly

There have been no specific clinical studies of Albumex® 4 in the elderly.

Genotoxicity

No genotoxicity studies have been conducted with Albumex® 4.

Carcinogenicity

No carcinogenicity studies have been conducted with Albumex® 4.

Effect on laboratory tests

Albumin is an endogenous plasma protein so no specific effects on laboratory tests are anticipated. However, administration of Albumex® 4 which may contain some bound bilirubin has been shown to result in elevated serum bilirubin in some patients.

INTERACTIONS WITH OTHER MEDICINES

Hypotension has been reported in patients given albumin who are on Angiotensin Converting Enzyme (ACE) inhibitors, (see also **Compatibility with other fluids**).

ADVERSE EFFECTS

Adverse reactions reported with albumin solutions in general may include chills, fever, flushing, headache, dyspnoea, nausea, vomiting, increased salivation and allergic reactions (hypotension, urticaria, skin rashes, anaphylaxis).

Adverse reactions to albumin solutions are uncommon and are usually mild and transient. More serious events may include rigors, hypotension, lowered serum electrolyte levels (potassium, calcium, bicarbonate), lowered total serum protein levels, low platelet count and increased prothrombin time.

DOSAGE AND ADMINISTRATION

Dosage

Hypovolaemia/shock

The management of hypovolaemic shock usually requires the intravenous (IV) infusion of at least one litre of Albumex® 4 into an average adult patient.

The total volume required cannot be accurately predicted, since it depends on such factors as the initial extracellular fluid volume deficit and the continuing rate of fluid loss.

Monitoring advice

It is recommended that blood pressure is monitored during administration of Albumex® 4.

To avoid circulatory overload the rate and volume of infusion should be monitored frequently.

Myocardial function should also be monitored e.g. central venous pressure, arterial pressure and pulse rate.

Myocardial function (in shock), serum potassium (when pretreatment concentrations are low), platelet count (when pretreatment values are low) and prothrombin times (when these are prolonged before exchange) should also be monitored.

Administration

CAUTION: Albumex® 4 contains no antimicrobial preservative. It must, therefore, be used immediately after opening the bottle. Any unused solution should be discarded appropriately. Use in one patient on one occasion only.

Albumex® 4 is normally clear or slightly opalescent. If it appears to be turbid by transmitted light, it must not be used and the bottle should be returned unopened to the New Zealand Blood Service.

Albumex® 4 should always be administered by intravenous infusion through a standard IV infusion giving set.

If the product was stored in the refrigerator it should be allowed to reach room temperature or body temperature before administration. Do not use if the solution has been frozen.

The following procedure is recommended:

1. Remove the plastic cover from the seal.
2. Apply a suitable antiseptic to the exposed part of the rubber stopper and allow to dry.
3. Stand the bottle upright and insert the air vent needle vertically in one of the indentations of the stopper. It is preferable to use a long airway needle fitted with a filter. If not available, a short needle attached to a non-wettable filter may be used.
4. Clamp the tubing of the giving set and insert the perforator vertically through one of the other indentations of the stopper. **Should the stopper become dislodged, do not use this bottle and discard the solution appropriately.**
5. Invert the bottle and attach the hanger to a support approximately one metre above the patient.
6. Allow the tubing to fill by adjusting the clamp. Insert the giving set needle into a vein and adjust the rate of flow.
7. When the bottle is empty, clamp the tubing and transfer the air vent needle and the needle at the upper end of the giving set to a further bottle of Albumex® 4 or to a bottle containing a crystalloid solution, according to requirements.
8. **Should leakage become evident during administration, cease the infusion and discard the solution appropriately. Recommence the infusion with a new bottle and giving set.**

Compatibility with other fluids

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.

OVERDOSAGE

Excess human albumin may lead to circulatory overload (see **PRECAUTIONS**).

PRESENTATION AND STORAGE CONDITIONS

Albumex® 4 is issued in three sizes:

- 2 g of human albumin in 50 mL of electrolyte solution
- 10 g of human albumin in 250 mL of electrolyte solution
- 20 g of human albumin in 500 mL of electrolyte solution.

Store below 30°C (Do not freeze). Protect from light. Do not use after the expiry date.

NAME AND ADDRESS OF THE SPONSOR

CSL Behring (NZ) Ltd
666 Great South Road
Penrose
Auckland
New Zealand

NAME AND ADDRESS OF THE MANUFACTURER

CSL Behring (Australia) Pty Ltd
189–209 Camp Road
Broadmeadows VIC 3047
Australia

NAME AND ADDRESS OF THE DISTRIBUTOR

New Zealand Blood Service
71 Great South Road
Epsom
Auckland
New Zealand

MEDICINE CLASSIFICATION

General Sale Medicine

DATE OF PREPARATION

09 May 2014

Albumex® is the registered trademark of CSL Limited

For Medical/Technical Enquiries

+61 3 9389 1932

For Customer Service Enquiries

+61 3 9246 5231

customerservice@cslbehring.com.au

www.cslbehring.com.au