

Albumex[®] 4

Human Albumin 4% (40 g/L)

New Zealand

NAME OF THE MEDICINE

Human albumin, solution for intravenous injection.

DESCRIPTION

Albumex[®] 4 is prepared from pooled human plasma obtained from voluntary donors. It is prepared by a combination of the Cohn cold-ethanol fractionation process and chromatographic techniques. It is a 4% w/v protein solution which is iso-osmotic with human serum. Albumex[®] 4 is heated at 60°C for 10 hours and incubated at low pH to inactivate viruses. The 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 20 days and the turnover in an adult is approximately 15g 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 (\pm SD) number of days spent in ICU (6.5 \pm 6.6 in the albumin group and 6.2 \pm 6.2 in the saline group, P=0.44), days spent in hospital (15.3 \pm 9.6 and 15.6 \pm 9.6 respectively, P=0.30), days of mechanical ventilation (4.5 \pm 6.1 and 4.3 \pm 5.7, respectively, P=0.74) or days of renal replacement therapy (0.5 \pm 2.3 and 0.4 \pm 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, however, 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

The product is normally clear or slightly opalescent but, if it appears to be turbid by transmitted light, it must not be used and the bottle should be returned unopened to the appropriate Blood Service.

Any case of infection associated with the use of the product should be reported to the appropriate Blood Service, together with details of batches given.

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).

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

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.

Albumex[®] 4 contains trace elements of aluminium ($\leq 200\mu\text{g/L}$). 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 drugs to Albumex[®] 4 has not been evaluated (See also **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 removal and inactivation procedures are included in the manufacturing process. The current procedures applied in the manufacture of this product are effective against enveloped viruses such as HIV (human immunodeficiency virus), hepatitis B and hepatitis C viruses, and the non-enveloped virus, hepatitis A. 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.

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.

Interactions with other medicines

Hypotension has been reported in patients given albumin who are on ACE (angiotensin - converting enzyme) 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 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. To avoid circulatory overload the rate and volume of infusion should be monitored frequently, e.g. by measurement of the central venous pressure, arterial pressure or pulse rate.

Administration

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

Albumex[®] 4 does not contain an 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. Do not use if the solution has been frozen. If the product was stored in the refrigerator it should be allowed to reach room temperature or body temperature before administration.

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:

- 2.0 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. This product must not be frozen. Protect from light. Do not use after the expiry date.

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MEDICINE CLASSIFICATION

General Sale Medicine

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Albumex[®] is the registered trademark of CSL Limited

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