**CSL Behring**

**Albumin (Human) 25% Solution**

**ALBURX® 25**

**DESCRIPTION**

ALBURX® 25, Albumin (Human) 25% solution is a sterile aqueous solution for intravenous administration containing the albumin component of human blood. The solution is clear and slightly viscous; it is almost colorless, or yellow, amber, or green. This product is prepared from the plasma of US donors. The product has been produced by alcohol fractionation and has been heated for 10 hours at 60°C for inactivation of infectious agents. The results of virus validation studies have shown that the manufacturing process, particularly alcohol fractionation, eliminates enveloped and non-enveloped viruses. Additionally, heat treatment at 60°C for a period of 10 hours efficiently inactivates viruses. The solution contains 0.14 M (3.2 mg/mL) sodium. The aluminum content is ≤ 200 mcg/mL and the potassium content is ≤ 0.002 M. The solution is stabilized with 0.02 M sodium N-acetyltryptophanate and 0.02 M sodium caprylate. The solution contains no preservative.

**CLINICAL PHARMACOLOGY**

ALBURX® 25, Albumin (Human) 25% solution should not be used as an intravenous nutrient because of the slow breakdown and relatively unfavorable composition of the albumin molecule with respect to its content of essential amino acids. Oral provision of proteins or an intravenous regimen providing adequate calories and a suitable amino acid mixture are the methods of choice for the treatment of protein malnutrition as such, though they do not permit the rapid correction of hypoproteinemia.

The binding properties of albumin may provide an indication for its use in severe hemolytic disease of the newborn, where it may lower the plasma concentration of free bilirubin pending an exchange transfusion. This effect is possibly also relevant in certain cases of acute liver failure with rapidly increasing levels of serum bilirubin, particularly in the presence of severe hypoproteinemia.

The colloid osmotic or oncotic properties of albumin at this moment constitute the predominant reason for its clinical use. The rationale for this is the Starling concept of the capillary balance of hydrostatic and oncotic pressure gradients across the capillary walls as the determinant of the fluid – i.e. volume – distribution between the intravascular and the interstitial compartment. The two main indications for the use of ALBURX® 25, Albumin (Human) 25% solution are therefore a plasma or blood volume deficit and the oncotic deficit resulting from hypoproteinemia. The 25% concentration is oncoticly equivalent to approximately five times its volume of normal human plasma. The effective colloid oncotic pressure of the serum proteins depends very largely on the relatively small and numerous albumin molecules, which therefore play a decisive role in the maintenance of the circulating plasma volume.

**INDICATIONS AND USAGE**

**General Principles**

**Volume Deficit**

Since the oncotic pressure of ALBURX® 25, Albumin (Human) 25% solution is about four times higher than that of normal human serum, it will expand the plasma volume if interstitial water is available for an inflow through the capillary walls. However, many patients suffering from an acute volume deficit also have some degree of interstitial dehydration. In the absence of hyperhydration, the treatment of an acute volume deficit with ALBURX® 25 should therefore include isotonic electrolyte solutions with an albumin:electrolyte ratio of 1:3 or 1:4. By contrast, chronic volume deficits have usually been at least partially compensated for by the renal retention of sodium and water with some degree of tissue edema, and in these circumstances a trial with ALBURX® 25 only is indicated. In any case, an anemia of clinically relevant magnitude requires specific treatment, and the metabolic needs of the patient with respect to fluid and electrolytes must be cared for.

**Oncotic Deficit**

The common causes of hypoproteinemia are protein-calorie malnutrition, definitive absorption in gastro-intestinal disorders, failure of albumin synthesis in chronic hepatic failure, increased protein catabolism postoperatively or with sepsis, and abnormal renal losses of albumin with chronic kidney disease. In all these settings, the circulating albumin mass is initially maintained by a gradual transfer of extravascular albumin to the circulation, and hypoproteinemia ensues only when this compensatory potential has been exhausted. This implies that manifest hypoproteinemia is usually accompanied by a hidden extravascular albumin deficit of equal magnitude as the measurable intravascular deficit, which must be allowed for if ALBURX® 25, Albumin (Human) 25% solution is infused because of the capillary permeability of that protein. The primary sequel of the oncotic deficit resulting from hypoproteinemia is a loss of plasma and a gain of interstitial volume with increased lymphatic flow. As a secondary response, the kidney retains sodium and water which distribute themselves on both sides of the capillary walls and the plasma volume may be returned almost to normal when the oncotic pressure increases sufficiently to compensate for the decrease of the serum oncotic pressure. This chain of events is accelerated by the infusion of crystalloid fluids. The plasma volume is maintained at the price of interstitial edema.

**Acute circumstances in which ALBURX® 25, Albumin (Human) 25% solution use is usually appropriate**

**Shock**

Though electrolyte solutions such as Ringer’s lactate and colloid-containing plasma substitutes may be used as an emergency treatment of shock, ALBURX® 25, Albumin (Human) 25% solution used according to the aforementioned principles has a much longer intravascular half-life and may therefore be preferable. In addition, anemia of clinically relevant magnitude requires specific therapy with red cells.

**Acute**

Immediate therapy during the first 24 hours is directed at the administration of large volumes of crystalloid solutions and lesser amounts of ALBURX® 25, Albumin (Human) 25% solution to maintain an adequate plasma volume and protein (colloid) content. For continuation of therapy beyond 24 hours, larger amounts of ALBURX® 25 and lesser amounts of crystalloid are generally used. An optimum regimen for the use of Albumin (Human), electrolytes, and fluid in the early treatment of burns has, however, not yet been established.

With restoration of normal capillary function, a close relationship exists once again between infused Albumin (Human) and resultant increase in plasma oncotic pressure. A goal should be sought of maintaining a plasma albumin concentration of about 2.5 ±0.5 g/100 mL or a plasma oncotic pressure of 20 mmHg (equivalent to a TSP of 25 ±0.5 g/100 mL). In the presence of extensive granulating wounds, a daily loss of up to 30 g of albumin may continue into the late post-burn period. Protein-rich oral feedings, or adequate parenteral nutrition should be included in the overall regimen to the fullest possible extent, though such treatment does not permit the rapid correction of an oncotic deficit.

**Acute circumstances in which ALBURX® 25, Albumin (Human) 25% solution use may be appropriate**

**Adult Respiratory Distress Syndrome**

Several factors are usually involved in the development of the state now commonly called the adult respiratory distress syndrome, one of these being a hypoproteinemic fluid overload. If present, this may be corrected by the use of ALBURX® 25, Albumin (Human) 25% solution and a diuretic.

**Cardiopulmonary Bypass**

An adequate blood volume during cardiopulmonary bypass can be maintained with crystalloids as the only pump priming fluid, but only at the price of interstitial edema. A commonly employed program is an ALBURX® 25, Albumin (Human) 25% solution and crystalloid pump prime adjusted so as to achieve a hematocrit of 20% and a plasma albumin level of 2.5 g/100 mL in the patient, but the level to which either may be lowered safely has not yet been defined.

**Third Space Problems of Infectious Origin**

The sequestration of protein-rich fluid during acute peritonitis, pancreatitis, mediastinitis or extensive cellulitis may be of sufficient magnitude to require the treatment of a volume or an oncotic deficit with ALBURX® 25, Albumin (Human) 25% solution, although this occurrence is relatively rare.

**Acute Liver Failure**

In acute liver failure, ALBURX® 25, Albumin (Human) may serve the triple purpose of stabilizing the circulation, correcting an oncotic deficit and binding excess serum bilirubin. The therapeutic approach is guided by the individual circumstances.

**Acute Nephrosis**

Patients undergoing major surgery may lose more than half of their circulating albumin mass, and complications attributable to an oncotic deficit may occur in such cases, as well as in septic and intensive care patients. Oncotic therapy with ALBURX® 25, Albumin (Human) 25% solution may therefore be indicated in such patients, according to the principles outlined in Oncotic Deficit. Temporary redistribution of protein is usually not an indication for Albumin (Human).
response may be elicited by combining 100 mL of 20–25% Albumin (Human) solution with an appropriate diuretic. This combination should be repeated daily for about one week, after which the patient may react satisfactorily to drug therapy. 1,7

Ascites
The use of ALBURX® 25, Albumin (Human) 25% solution for blood volume support may be indicated if circulatory instability follows the withdrawal of ascitic fluid.

Red Cell Resuspension Media
As a rule, the use of Albumin (Human) for resuspending red cells can be dispensed with. However, in exceptional circumstances such as certain types of exchange transfusions and the use of very large volumes of erythrocyte concentrates and frozen or washed red cells, the addition of ALBURX® 25, Albumin (Human) 25% solution to the resuspension medium may be indicated in order to provide sufficient volume and/or to avoid excessive hypoproteinemia during the subsequent transfusion. If necessary, 20–25 g or more of Albumin (Human) per liter of red cell suspension should be added as a concentrated solution to the isotonic, electrolyte suspension of erythrocytes immediately before transfusion, the individual dosage depending on the TSP level of the recipient.

Renal Dialysis
Patients undergoing long-term hemodialysis may need ALBURX® 25, Albumin (Human) 25% solution for the treatment of a volume or an oncotic deficit. As a rule, the initial dose should not exceed 100 mL of a 20–25% solution, and the patients should be carefully observed for signs of a circulatory overload, to which they are particularly sensitive.

Hemolytic Disease of the Newborn
ALBURX® 25, Albumin (Human) 25% solution may be indicated in order to bind and thus detoxify free serum bilirubin in severely hemolytic infants pending an exchange transfusion. Circumstances in which ALBURX® 25, Albumin (Human) 25% solution use is not justified for the reasons set forth in sections CLINICAL PHARMACOLOGY and General Principles, there is no valid reason for the use of ALBURX® 25, Albumin (Human) 25% solution as an intravenous nutrient or for treating the stabilized hypoproteinemia accompanying chronic cirrhosis, chronic nephrosis, protein-losing enteropathy, malabsorption and pancreatic insufficiency.

If, however, the patient in this category has to cope with a superimposed acute stress, the prescription of an appropriate diuretic for the treatment of ascites and edema makes sense in order to prevent circulatory overload, to which the patient is particularly sensitive.

CONTRAINDICATIONS
The only specific contraindication to the use of ALBURX® 25, Albumin (Human) 25% solution is the presence of an anaphylactic reaction to Albumin (Human) in the individual recipient (see ADVERSE REACTIONS).

WARNINGS
ALBURX® 25, Albumin (Human) 25% solution is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been extremely reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current viral infections, and by inactivating and/or removing certain viruses through alcohol fractionation and through heat treatment of the product in the final container for 10 hours at 60°C. Despite these measures, such products can still potentially transmit disease. A theoretical risk for transmission of Creutzfeldt-Jakob Disease (CJD) is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for Albumin (Human). There is also the possibility that unknown infectious agents may be present in such products. All infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to CSL Behring Pharmacovigilance Department at 1-866-915-6958. The physician should discuss the risks and benefits of this product with the patient.

Turbid solutions must not be used. Do not begin administration more than 4 hours after introduction of the administration set. There exists a risk of potentially fatal hemolysis and acute renal failure from the inappropriate use of sterile water for injection as a diluent for ALBURX® 25, Albumin (Human) 25% solution. Acceptable diluents include 0.9% sodium chloride or 5% dextrose in water.

PRECAUTIONS
Adequate precautions should be taken against bacterial overload and may include pulmonary auscultation or X-ray as well as monitoring the central venous or pulmonary artery wedge pressure. Special caution is indicated in patients with stabilized chronic anemia, congestive heart failure and renal insufficiency.

Pregnancy
Animal reproduction studies have not been conducted with ALBURX® 25, Albumin (Human) (25% solution). It is also not known whether ALBURX® 25 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. ALBURX® 25 should be given to a pregnant woman only if clearly needed. There is, however, no evidence for any contraindication to the use of ALBURX® 25 specifically associated with reproduction, pregnancy or the fetus.

Use an intravenous infusion set suitable for the infusion of blood and blood products.

ADVERSE REACTIONS
Since ALBURX® 25, Albumin (Human) 25% solution is sterile when coming from the manufacturer, bacterial contamination with the risk of post-infusion sepsis can only occur if the container has been damaged or following puncture of the rubber cap (see Warnings). Though very rare, non-septic incompatibility reactions including nausea, chills, fever, urticaria, headache and hypotension following the administration of albumin-containing preparations have been recorded.11,12,13 A favorable response was observed to the intravenous administration of 50 to 100 mg of prednisolone.12 Severe allergic reactions, such as anaphylactic shock, have been reported.

DOSEAGE AND ADMINISTRATION
ALBURX® 25, Albumin (Human) 25% solution must be administered intravenously. The venipuncture site should not be infected or traumatized, and should be prepared with standard aseptic technique. The solution is compatible with whole blood or packed red cells as well as the usual electrolyte and carbohydrate solutions intended for intravenous use. By contrast, it should not be mixed with protein hydrolysates, amino acid mixtures, or solutions containing alcohol. It is ready for use as contained in the bottle and may be given without regard to the blood group of the recipient.

The dosage of ALBURX® 25, Albumin (Human) 25% solution is based on the principles outlined in the section on INSTRUCTIONS AND USAGE but should always be adapted to the individual situation. The quantities required may be underestimated because of hidden extravascular deficits, and the effect of ALBURX® 25 infusion on the serum protein level should therefore be checked by laboratory analysis.

Volume Deficit
The appropriate ALBURX® 25, Albumin (Human) 25% solution dose for the treatment of a volume deficit should be estimated from the recipient’s hemodynamic response, supplemented with the established safeguards against a circulatory overload. In the absence of active hemorrhage, the total dose should not be allowed to exceed the normal circulating albumin mass, i.e. 2 g per kg body weight.

Oncotic Deficit
The appropriate ALBURX® 25, Albumin (Human) 25% solution dose for the correction of an oncotic deficit can, as an average, be estimated from the difference between the desired and the actual TSP level x plasma volume (40–50 mL/kg) x 2, the latter factor allowing for the hidden extravascular deficit. The individual effect is, however, variable and should be checked by measuring the post-infusion TSP level.14,15

Hemolytic Disease of the Newborn
The appropriate ALBURX® 25, Albumin (Human) 25% solution dose for the binding of free serum bilirubin in severely hemolytic infants is 1 g/kg body weight, to be given about one hour prior to the exchange transfusion, and caution is recommended in hypoalbuminemic infants.

ALBURX® 25, Albumin (Human) 25% solution is clear and slightly viscous; it is almost colorless, or yellow, amber, or green. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use solution that is turbid or contains particulate matter. Partially used bottles must be discarded.

HOW SUPPLIED
ALBURX® 25 is supplied as a 25% solution (250 g/L). Each product presentation includes a package insert and the following components listed in Table 1 below.

Table 1. How Supplied

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Carton Number</th>
<th>Components</th>
</tr>
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<tbody>
<tr>
<td>50 mL</td>
<td>44206-251-05</td>
<td>One single-dose vial containing 12.5 g of albumin [NDC 44206-251-90]</td>
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<tr>
<td>100 mL</td>
<td>44206-251-10</td>
<td>One single-dose vial containing 25 g of albumin [NDC 44206-251-91]</td>
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STORAGE
ALBURX® 25, Albumin (Human) 25% solution should be stored at a temperature not exceeding 30°C (86°F). It should not be used after the expiration date printed on the label.

REFERENCES
2. Cavena AL, Moss G. J. Trauma. 1974;14:386.