edema.2

When the interstitial hydrostatic pressure increases sufficiently to compensate for the
plasma and a gain of interstitial volume with increased lymphatic flow. As a secondary

The primary sequel of the oncotic deficit resulting from hypoproteinemia is a loss of
solution is infused because of the capillary permeability of that protein.

been exhausted. This implies that manifest hypoproteinemia is usually accompanied
the circulation, and hypoproteinemia ensues only when this compensatory potential has

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
intravascular water is available to flow 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
diafiltrate 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 is
indicated. In any case, 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, defective
absorption in gastro-intestinal disorders, faulty 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
cells of the capillary walls and the plasma volume may be returned almost to normal
when the interstitial hydrostatic 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.2 There is some evidence that a serum oncotic pressure near 20 mmHg – equaling a total
serum protein (TSP) concentration of 5.2 g/100 mL – represents a threshold, below
which the risk of complications increases.17 The target organs of hypoproteinemia
include the skin, the lungs, and the intestine.16 Cutaneous edema lowers the oxygen
tension of wounds and may thus impair the healing process.17 An oncotic deficit favors
fluid development of intestinal pulmonary edema” and the intestinal accumulation of
fluids, which may progress to a paralytic ileus.9

Relief of the basic pathology is the definitive mode of therapy for the restoration of
the plasma protein content, but this process takes time to become effective, and the rapid
correction of a critical oncotic deficit by the administration of AlbuRx® 25, Albumin
(Human) 25% solution – possibly in conjunction with a diuretic – may therefore be
indicated, particularly in high-risk patients who have undergone abdominal, cardio-
vascular, thoracic, or urologic surgery or who have acute bacteremia. In notably
caabolic patients, attempts to raise the TSP level above 6 g/100 mL usually prove
futile, even with massive doses of Albumin (Human).15 It is emphasized that whereas AlbuRx® 25, Albumin (Human) 25% solution may be
necessary to prevent or treat the aforementioned acute complications of
hypoproteinemia, it is not indicated for treatment of the chronic condition itself.

Specific Indications
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.

Burns
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.13 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
25.0 -2.5 g/100 mL or a plasma oncotic pressure of 20 mmHg (equivalent to a TSP
concentration of about 5.2 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.1
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 hypoproteinemian
fluid overload. If present, this may be corrected by the use of AlbuRx® 25, Albumin
(Human) 25% solution and a diuretic.1,17

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.11

Pre- and postoperative Hypoproteinemia
Patients undergoing major surgery may lose more than half of their circulating albumin
mass6,9,15, and complications attributable to an oncotic deficit may occur in such cases,

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%
solution1, although this occurrence is relatively rare.

Acute Liver Failure
In acute liver failure, AlbuRx® 25, Albumin (Human) 25% solution may serve the triple
purpose of stabilizing the circulation, correcting an oncotic deficit and binding excessive
serum bilirubin. The therapeutic approach is guided by the individual circumstances.12

Acute Nephrosis
Patients with acute nephrosis may prove refractory to cyclophosphamide or steroid
therapy and their edema may even be aggravated initially by steroids. In such cases, a

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.14 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 oncotically equivalent to approximately five times its volume of normal
human plasma. The effective colloid osmotic 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
intravascular water is available to flow 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
diafiltrate 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 is
indicated. In any case, 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, defective
absorption in gastro-intestinal disorders, faulty 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
cells of the capillary walls and the plasma volume may be returned almost to normal
when the interstitial hydrostatic 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.2
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.17

Ascites
The use of AlbuR® 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 AlbuR® 25, Albumin (Human) 25% solution to the resuspension medium may be indicated in order to provide sufficient volume and/or 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 AlbuR® 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
AlbuR® 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 AlbuR® 25, Albumin (Human) 25% solution use is not justified For the reasons set forth in CLINICAL PHARMACOLOGY and General Principles, there is no valid reason for the use of AlbuR® 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, a patient in this category has to cope with a superimposed acute stress, pancreatic insufficiency.

Contraindications
The only specific contraindication to the use of AlbuR® 25, Albumin (Human) 25% solution is a history of an incompatibility reaction to Albumin (Human) in the individual recipient (see ADVERSE REACTIONS).

Warnings
AlbuR® 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 virus 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 thus 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.

Tubid solutions must not be used. Do not begin administration more than 4 hours after introduction of the administration set. Partially used bottles must be discarded. 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 AlbuR® 25, Albumin (Human) 25% solution. Acceptable diluents include 0.9% sodium chloride or 5% dextrose in water.

Precautions
Adequate precautions should be taken against circulatory 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 Category C
Animal reproduction studies have not been conducted with AlbuR® 25, Albumin (Human) 25% solution. It is also not known whether AlbuR® 25 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. AlbuR® 25 should be given to a pregnant woman only if clearly needed. There is, however, no evidence for any contraindication to the use of AlbuR® 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 AlbuR® 25, Albumin (Human) 25% solution is sterile when coming from the manufacturer, bacterial contamination with the risk of post-infusion septicemia can only occur if the container has been damaged or following puncture of the rubber cap

(see WARNINGS).

Dose and Administration
AlbuR® 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 AlbuR® 25, Albumin (Human) 25% solution is based on the principles outlined in the section on indications 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 AlbuR® 25 infusion on the serum protein level should therefore be checked by laboratory analysis.

Volume Deficit
The appropriate AlbuR® 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 at any rate not exceed the normal circulating albumin mass, i.e. 2 g per kg body weight.

Oncotic Deficit
The appropriate AlbuR® 25, Albumin (Human) 25% solution dose in grams of protein 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 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.16,17

Hemolytic Disease of the Newborn
The appropriate AlbuR® 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 hypervolemic infants.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

How Supplied
AlbuR® 25 is supplied as a 25% solution (250 g/l).

Each product presentation includes a package insert and the following components:

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Carton NDC Number</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 mL</td>
<td>44206-251-05</td>
<td>One vial containing 12.5 gms of albumin (NDC 44206-251-90)</td>
</tr>
<tr>
<td>100 mL</td>
<td>44206-251-10</td>
<td>One vial containing 25 gms of albumin (NDC 44206-251-31)</td>
</tr>
</tbody>
</table>

Storage
AlbuR® 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

Manufactured by: CSL Behring AG
Benn, Switzerland
Distributed by: CSL Behring LLC
Kankakee, IL 60901 USA
Revised: August 2012