CSL Behring

Name of the medicinal product
AlbuRx™ 25

Composition
a. Active substance
Human albumin
Human plasma protein with albumin content of at least 95%.

b. Excipients

Sodium N-acetyltryptophanate	20 mmol/l
Sodium caprylate	20 mmol/l
Sodium chloride	q.s. to a sodium content of 140 mmol/l
Water for injections	q.s. to 1 l
Aluminium content	≤ 200 µg/l

AlbuRx™ 25 complies with the European Pharmacopoeia upper limit for the aluminium content of human albumin solutions for infusions (maximum 200 micrograms/l).

AlbuRx™ 25 contains approximately 3.2 mg sodium per ml of solution (140 mmol/l).

Pharmaceutical form and active substance content per unit
Solution for intravenous infusion.
The solution contains 250 g/l of human plasma protein, of which at least 95% is albumin.

AlbuRx™ 25 is an almost colourless, yellow, amber, or green solution for infusion.

It is hyperoncotic to normal plasma.

Therapeutic indications
Restoration and maintenance of circulating blood volume in cases of volume deficiency where the use of a colloid is indicated.
The choice of albumin rather than artificial colloid will depend on the clinical situation of the individual patient, based on official recommendations.

Posology/ Method of administration
The concentration of the albumin solution used, the dosage and the infusion rate should be adjusted to the patient's individual requirements.

Posology
The dose required depends on the size of the patient, the severity of trauma or illness and on continuing fluid or protein losses. Measurements of the circulating blood volume, and not just of the plasma albumin level, should be used to determine the dose required.

Human albumin should be administered under careful haemodynamic monitoring; the parameters include:
- arterial blood pressure and heart rate,
- central venous pressure,
- pulmonary artery wedge pressure,
- urine output,
- electrolytes,
- haematocrit / haemoglobin.

Paediatric population
The posology in children and adolescents (0-18 years) should be adjusted to the patient's individual requirements.

Method of administration
AlbuRx^{TM} 25 is administered intravenously.

The product is ready for use and can be administered as supplied, either directly or it can first be diluted to 5% albumin with an isotonic solution (e.g. 5% glucose or 0.9% sodium chloride). The infusion rate should be adjusted according to the individual circumstances and the indication, but should normally not exceed 1 - 2 ml/min.
In plasma exchange the infusion rate should be adjusted to the rate of removal.

The diluted solution is a clear, slightly viscous and almost colourless, yellow, amber, or green solution. The diluted product is stable for 24 hours at 30^0C

Contraindications
Hypersensitivity to albumin preparations or to any of the excipients (see section "Composition").

Warnings and precautions for use
In the event of allergic or anaphylactic type reactions the infusion must be discontinued immediately and appropriate treatment must be instituted. In case of anaphylactic shock, the current medical guidelines for shock should be followed.

Albumin should be used with caution in all conditions where hypervolaemia and its consequences or haemodilution could represent a special risk for the patient. Examples of such conditions are:
- Congestive cardiac failure,
- Hypertension,
- Oesophageal varices,
- Pulmonary oedema,
- Hemorrhagic diathesis,
- Severe anaemia,
- Renal or postrenal anuria.

The colloid-osmotic effect of human albumin 250 g/l is approximately four times that of blood plasma. Therefore, when concentrated albumin is administered, care must be taken to assure adequate hydration of the patient. Patients should be monitored carefully to guard against circulatory overload and hyperhydration.

250 g/l human albumin solutions are relatively low in electrolytes compared to the 40 - 50 g/l albumin solutions. When albumin is given, the electrolyte status of the patient should be monitored and appropriate steps taken to restore or maintain the electrolyte balance.

Albumin solutions must not be diluted with water for injections as this may cause haemolysis in patients.

If comparatively large volumes are to be replaced, controls of coagulation and haematocrit are necessary. Care must be taken to ensure adequate substitution of other blood constituents (coagulation factors, electrolytes, platelets and erythrocytes).

Hypervolaemia may occur if the dosage and infusion rate are not adjusted to the patient's circulatory situation. At the first clinical signs of cardiovascular overload (headache, dyspnoea, jugular vein congestion), or in the event of increased blood pressure, raised central venous pressure or pulmonary oedema, the infusion must be stopped immediately and the patient's haemodynamic parameters must be carefully monitored.

AlbuRx^{TM} 25 contains approximately 3.2 mg sodium per ml of solution (140 mmol/l). That should be taken into consideration for patients on a controlled sodium diet.

Information on safety in regard to transmissible agents
Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

Albumin manufactured to European Pharmacopoeia specifications is regarded as having reliable viral safety.

It is recommended that every time AlbuRx^{TM} 25 is administered to a patient, the name and batch number of the product should be recorded in order to create a link between the patient and the batch of the product.

Interactions
No specific interactions between human albumin and other medicinal products are known. However, it should be borne in mind that the effects of medicinal products that bind strongly to albumin may be influenced by changes in the albumin level.

Pregnancy and lactation
No controlled clinical studies on the use of AlbuRx^{TM} 25 in humans during pregnancy are available. However, clinical experience with albumin has not yet given rise to any evidence of harmful effects on the course of pregnancy, to the fetus, or to the neonate. No animal reproduction studies have been conducted with AlbuRx^{TM} 25. However, human albumin is a normal constituent of human blood.

Effect on the ability to drive and use machines
There is no evidence of adverse effects affecting the ability to drive or use machines.

Undesirable effects

Summary of the safety profile

Mild reactions such as flush with heat sensation, urticaria, fever and nausea occur rarely. These reactions normally disappear rapidly when the infusion rate is slowed down or the infusion is stopped. In very rare cases, severe allergic reactions such as anaphylactic shock can occur. In these cases, the infusion must be stopped and an appropriate treatment must be initiated.

Adverse reactions after launch

The adverse reactions presented in the following have been observed with AlbuRx^{TM} 25 during the postmarketing phase and are summarised and categorised according to MedDRA system organ classification and frequencies.

As the postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not possible to reliably estimate the frequency of these reaction. Hence the frequency category "not known (cannot be estimated from the available data)" is used.

Immune system disorders: hypersensitivity reactions (including anaphylaxis and shock)

Gastrointestinal disorders: nausea

Skin and subcutaneous tissue disorders: flush, urticaria

General disorders and administration site conditions: fever

For information concerning viral safety, see section "Warnings and precautions for use".

Overdose

Hypervolaemia may occur if the dosage and infusion rate are too high. At the first clinical signs of cardiovascular overload (headache, dyspnoea, jugular vein congestion), or in the event of increased blood pressure, raised central venous pressure or pulmonary oedema, the infusion must be stopped immediately and the patient's haemodynamic parameters must be carefully monitored.

Properties/effects

ATC code: B05AA01.

Pharmacotherapeutic group: Plasma substitutes and plasma protein fractions.

Albumin accounts quantitatively for more than 50% of the total protein in the plasma and represents about 10% of the protein synthesis activity of the liver.

Mechanism of action/ Pharmacodynamics

The most important physiological functions of albumin results from its contribution to oncotic pressure of the blood and its transport function. Albumin stabilizes circulating blood volume and is a carrier of hormones, enzymes, drugs, and toxins.

Pharmacokinetics

Distribution
Under normal conditions, the total exchangeable albumin pool is 4 – 5 g/kg body weight, of which 40 – 45% is present intravascularly and 55–60% in the extravascular space. Increased capillary permeability alters albumin kinetics. Abnormal distribution can occur under pathological conditions, e.g. after severe burns and in septic shock.

Elimination
Under normal conditions, the average half-life of albumin is about 19 days. The balance between synthesis and breakdown is normally achieved by a feedback mechanism. Elimination is predominantly intracellular and due to lysosomal proteases.

In healthy subjects, less than 10% of infused albumin leaves the intravascular compartment during the first 2 hours following infusion. There is considerable individual variation in the effect on plasma volume. In some patients the plasma volume remains increased for several hours. However, in critically ill patients, albumin can leak out of the vascular system in substantial amounts at an unpredictable rate.

Preclinical data
Human albumin is a normal constituent of human plasma and its action does not differ from that of physiological albumin.

Single dose toxicity testing in animals is of little relevance and does not permit the evaluation of toxic or lethal doses or of a dose-effect relationship. It is not possible to carry out repeated dose toxicity testing in animals due to the development of antibodies to heterologous proteins.

To date, human albumin has not been reported to be associated with embryo-fetal toxicity, mutagenic, or carcinogenic potential. No signs of acute toxicity have been described in animal models.

Other information
Incompatibilities
AlbuRx^{TM} 25 must not be mixed with other medicinal products, including whole blood and packed red cells.

Shelf life and special storage conditions
3 years.
Do not use AlbuRx^{TM} 25 after the expiry date which is stated on the outer carton and the vial label after "EXP". Do not store AlbuRx^{TM} 25 above 30°C. Do not freeze. Keep the vial in the outer carton in order to protect from light.
Keep out of the reach of children.

Instructions for use and handling
AlbuRx^{TM} 25 is administered intravenously.

Albumin solutions must not be diluted with water for injections as this may cause haemolysis in patients.

If large volumes are administered, the product should be warmed to room or body temperature before use.

The solution is clear and slightly viscous. Do not use infusion solutions that are cloudy or have deposits. This may indicate that the protein is unstable or that the solution has become contaminated.

Once the container has been opened, the contents should be used immediately. Any unused product or waste material should be disposed of in accordance with local regulations.

Packs
AlbuRx™ 25 single use vial glass type II (Ph. Eur.)

- 12.5 g/ 50 ml
- 25 g/ 100 ml

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Switzerland

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