PRODUCT MONOGRAPH

Alburex® 5
Alburex® 25

Albumin (Human) USP

5% Solution for Infusion
25% Solution for Infusion

Plasma Substitute/Blood Derivative

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Table of Contents

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form/ Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous	Solution for infusion: 5% (50 g/L) and 25% (250 g/L)	Sodium N-acetyltryptophanate, Sodium caprylate, Sodium chloride, Water for injection. *See below for a complete list of excipients.*

List of excipients

Alburex® 5 (50 g/L)

Sodium N-acetyltryptophanate

Sodium caprylate

Sodium chloride

Water for injection

Alburex® 25 (250 g/L)

Sodium N-acetyltryptophanate

Sodium caprylate

Sodium chloride

Water for injection

DESCRIPTION

Alburex® 5 and Alburex® 25, Albumin (Human), are sterile aqueous solutions of albumin obtained from large pools of adult human venous plasma by low temperature controlled fractionation according to the Cohn process modified by Kistler Nitschmann. It is stabilized with sodium acetyltryptophanate and sodium caprylate and pasteurized at 60°C for at least 10 hours.

Alburex® 5, Albumin (Human) solution for infusion is mildly hypooncotic to normal human plasma and contains, in each 100 mL, 5 grams of protein, of which at least 96% is human albumin.

Alburex® 25, Albumin (Human) solution for infusion is hyperoncotic to normal human plasma and contains, in each 100 mL, 25 grams of protein, of which at least 96% is human albumin.

The pH of the solution is adjusted as needed with hydrochloric acid or sodium hydroxide. Approximate concentrations of significant electrolytes per liter are: 0.14 M sodium; and the potassium content is ≤ 0.002M. The solution contains no preservative.

Alburex® solutions should be administered intravenously.

This product has been prepared in accordance with the requirements established by the Food and Drug Administration and is in compliance with the standards of the United States Pharmacopoeia.

INDICATIONS AND CLINICAL USE

Alburex® 5 and Alburex® 25, Albumin (Human), are indicated for:

Restoring and maintaining circulating blood volume, based on albumin's oncotic and colloid-osmotic properties. The choice of albumin over artificial colloid and crystalloid solutions should be made according to current medical practice. Please refer to the **DOSAGE** and **ADMINISTRATION** section for concentration specific modes of administration.

SHOCK – Alburex® is indicated in the emergency treatment of shock and in other similar conditions where the restoration of blood volume is urgent. In conditions associated mainly with a volume deficit, albumin is best administered as a 5% solution; but where there is an oncotic deficit, the 25% solution may be preferred. If there has been considerable loss of red blood cells, transfusion with packed red blood cells is indicated.

BURNS – Alburex® in combination with crystalloid solutions is used to maintain adequate plasma volume and protein content.

HYPOPROTEINEMIA with or without edema – Alburex® is indicated in those clinical situations usually associated with a low concentration of plasma protein and a resulting decreased circulating blood volume. Measures of adequacy of circulating volume and not plasma albumin levels should be used to determine the dose required. Albumin (Human) is not indicated as nutrient in the treatment of chronic hypoproteinemia.

Pediatrics:
No clinical studies using Alburex® have been conducted in pediatric patients. Safety and effectiveness in pediatric patients have not been established. However, extensive experience in patients suggests that children respond to Alburex® in the same manner as adults.

CONTRAINDICATIONS

Alburex® 5 and Alburex® 25, Albumin (Human), are contraindicated in patients who are hypersensitive to human albumin or to any ingredient in the formulation or component of the container. For a complete listing of ingredients, see the **DESCRIPTION** section.

Alburex® is contraindicated in patients with severe anemia or cardiac failure.

WARNINGS AND PRECAUTIONS

General

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the infusion. In case of shock, standard medical treatment for shock should be implemented.

Alburex® 5 and Alburex® 25, Albumin (Human), should be used with caution in conditions where hypervolemia and its consequences or hemodilution could represent a special risk for the patient. Examples of such conditions are:

- decompensated cardiac insufficiency
- hypertension
- esophageal varices
- pulmonary edema
- hemorrhagic diathesis
- severe anemia
- renal and post-renal anuria

The colloid-osmotic effect of 250 g/L Albumin (Human) 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 Albumin (Human) solutions are relatively low in electrolytes compared to the 50 g/L Albumin (Human) solutions. When albumin is given, the electrolyte status of the patient should be monitored (see **DOSAGE AND ADMINISTRATION** section) and appropriate steps taken to restore or maintain the electrolyte balance.

Protein-containing solutions such as Alburex® must not be diluted with hypotonic solutions such as sterile water for injection, as this may result in severe hemolysis and acute renal failure. Please refer to the **DOSAGE AND ADMINISTRATION** section for information about the recommended diluents for Alburex®.

Albumin (Human) contains approximately 3.2 mg sodium per ml of solution (0.14 M), which should be taken into consideration for patients on a controlled sodium diet.

Alburex® is made from human plasma. Standard measures to prevent infections resulting from 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 inclusion of effective manufacturing steps for 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 (i.e. parvovirus B19 which may affect pregnant women or immune compromised individuals). This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as HIV, HBV, HCV and for the non-enveloped viruses HAV and parvovirus B19.

A theoretical risk for transmission of variant Creutzfeldt Jacob disease (vCJD) is considered extremely remote.

There are no reports of proven virus transmissions with albumin manufactured to European or US pharmacopoeia specifications by established CSL processes.

Any infection thought by a physician to possibly have been transmitted by this product, should be reported by the physician or other healthcare provider to CSL Behring Canada, Inc. at 1-613-783-1892. The physician should discuss the risks and benefits of this product with the patient.

Effect on ability to drive and use machines: No effects on the ability to drive and use machines have been observed.

Hematologic

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

Cardiovascular

The colloid-osmotic effect of 250 g/L Albumin (Human) is approximately four times that of blood plasma. Therefore, care must be taken to assure adequate hydration of the patient when administering Alburex®. Patients should be monitored carefully to guard against circulatory overload and hyperhydration. Hypervolemia may occur if the dosage and infusion rate are not adjusted to the patient's circulatory situation.

Alburex® should be administered with caution to patients with low cardiac reserve. At the first clinical signs of cardiovascular overload (headache, dyspnea, jugular vein congestion), or increased blood pressure, raised venous pressure or pulmonary edema, the infusion is to be stopped immediately and the patient's haemodynamic parameter carefully monitored.

Sexual Function/Reproduction

It is not known whether Alburex® can affect reproduction capacity. No animal reproduction studies have been conducted with Alburex®. However, human albumin is a normal constituent of human blood and harmful effects on fertility are not expected.

Special Populations

Pregnant Women: No animal reproduction studies have been conducted with Alburex®. Its safety for use in human pregnancy has not been established in controlled clinical trials and therefore it should only be given with caution to pregnant women. However, clinical experience with human albumin suggests that no harmful effects on the course of pregnancy, or on the fetus and the neonate are to be expected.

Nursing Women: It is unknown whether Alburex® is excreted in human milk. It should then only be given with caution to nursing/breastfeeding women. However, since human albumin is a normal constituent of human blood, treatment of the nursing mother with Alburex® is not expected to present a risk to the breastfed newborn/infant.

Pediatrics: No clinical studies using Alburex® have been conducted in pediatric patients. Safety and effectiveness in pediatric patients have not been established. However, extensive experience in patients suggests that children respond to Alburex® in the same manner as adults.

Monitoring and Laboratory Tests

Refer to the Hematologic Subheading.

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

The Cochrane Collaboration examined 30 previously published albumin studies, involving a total of 1,419 patients. The authors included randomized trials that enrolled critically-ill patients who were hypovolemic or hypoalbuminemic and treated with albumin, plasma protein fraction or crystalloids. The intent of the authors was to compare outcomes with the albumin and plasma protein fraction with that of crystalloids. The results, published in 1998 (BMJ 1998; 317: 235-40), suggested that the mortality rates were higher in the patient groups treated with albumin or plasma protein fraction than in the groups treated with crystalloids. However, this meta-analysis has been challenged due to the heterogeneity of the patient populations studied, the inclusion of poor-quality and old studies not reflecting current practice, and the use of studies with unpublished data and/or patient populations that were too small to be meaningful. In addition, this meta-analysis was not an appropriate tool to compare albumin vs. crystalloids, since this type of analysis are used to generate hypotheses, rather than to prove hypotheses.

A larger, rigorous meta-analysis by Wilkes and Navickis, published in 2001 (Ann Intern Med 2001; 135: 149-64), which included additional studies with larger patient populations did not reproduce the results of the Cochrane group and suggests on the contrary that albumin may reduce mortality.

The recent Saline versus Albumin Fluid Evaluation study (The SAFE Study Investigators, NEJM 2004; 350: 2247-56) was designed to provide a definitive answer to the questions raised by the Cochrane report. This was a double-blind study which effectively captured all critically-ill patients receiving volume resuscitation in Australia. The study randomized 6997 patients, of whom 3497 were treated with 4% albumin and 3500 with normal saline. The primary outcome measure was mortality at 28 days, but the authors also examined time spent in the ICU, time spent in hospital, requirements for mechanical ventilation and requirements for renal dialysis. The study found no significant differences in any study outcome in the first 28 days of stay in the intensive care unit. This study, by far the largest study ever done with albumin, showed that there was no additional mortality due to the use of albumin.

A greater number of patients with trauma involving brain injury died among those randomly assigned to albumin as opposed to saline (59 of 241 in the albumin group compared to 38 of 251 in the saline group with a relative risk of 1.62 and p=0.009). However, the overall number of these patients was relatively small. The study had insufficient power to detect differences in mortality among the predefined subgroups and the authors warn that the observed difference should be interpreted with caution.

Post-Market Adverse Drug Reactions

The incidence of untoward reactions to Alburex® 5/Alburex® 25, Albumin (Human) is low. Mild reactions such as flush, urticaria, fever and nausea occur rarely. These reactions normally disappear rapidly when the infusion rate is slowed down or the infusion is stopped. Reports have been received of anaphylaxis, which may be severe, and hypersensitivity reactions (including urticaria, skin rash, pruritus, edema, erythema, hypotension and bronchospasm).Very rarely, severe allergic reactions such as anaphylactic shock may occur. In these cases, the infusion should be stopped immediately and an appropriate treatment should be initiated.

For safety with respect to transmissible agent, see **WARNINGS AND PRECAUTIONS** and **PHARMACEUTICAL INFORMATION**.

DRUG INTERACTIONS

No specific interactions of Alburex® 5/Alburex® 25, Albumin (Human) with other medicinal products are known. However, the effects of medicinal products with extensive binding to albumin may be impacted by changes in circulating albumin levels.

Incompatibilities

Alburex® 5 and Alburex® 25, Albumin (Human), solutions for infusion must not be mixed with other medicinal products (except those mentioned in **DOSAGE AND ADMINISTRATION** section) including whole blood and packed red cells.

DOSAGE AND ADMINISTRATION

Alburex®, Albumin (Human) is a ready-to-use solution and should be administered by the intravenous route only. Alburex® 25 can also be diluted in an isotonic solution of e.g. 5% glucose or 0.9% sodium chloride. Alburex® 5/Alburex® 25, Albumin (Human) solution for infusion must not be diluted with water for injection as this may cause hemolysis in recipients.

Recommended Dose, Dosage Adjustment and Administration

The concentration of the albumin preparation, dosage and the infusion-rate should be adjusted to the patient's individual requirements. The infusion rate should normally not exceed 5 mL/min for Alburex® 5 or 1-2 mL/min for Alburex® 25, Albumin (Human). Care must be taken to ensure adequate substitution of other blood components (coagulation factors, electrolytes, platelets and erythrocytes).

Alburex® 5

Alburex® 5, 50 g/L Albumin (Human) is a ready-to-use solution and should be administered by the intravenous route only. This concentration is approximately isotonic and iso-osmotic with citrated plasma. Albumin (Human) in this concentration provides additional fluid for plasma volume replacement. Therefore, when it is administered to patients with normal blood volume, the rate of infusion should be slow enough to prevent too rapid increase of plasma volume.

The dose should be adjusted based on patient's body weight, severity of treated condition, and estimated fluid and protein loss as determined by monitoring hemodynamic parameters, circulating volume and plasma protein levels, to avoid complications related to potential hypervolemia.

SHOCK: Therapy should be guided by the patient's response.

BURNS: In the treatment of burns, an optimal regimen involving use of albumin, crystalloids, electrolytes and water has not been established. Suggested therapy during the first 24 hours includes administration of large volumes of crystalloid solution to maintain an adequate plasma volume. After the first 24 hours, the ratio of albumin to crystalloid may be increased to establish and maintain a plasma albumin level of about 2.5 g/100 mL or a total serum protein level of about 5.2 g/100 mL. Duration of treatment varies depending upon the extent of protein loss through renal excretion, denuded areas of skin and decreased albumin synthesis.

HYPOPROTEINEMIA: The infusion of Albumin (Human) as a nutrient in the treatment of chronic hypoproteinemia is not recommended. In acute hypoproteinemia, 50 g/L Albumin (Human) may be used in replacing the protein lost in hypoproteinemic conditions. However, if edema is present or if large amounts of albumin are lost, 250 g/L Albumin (Human) is preferred because of the greater amount of protein in the concentrated solution.

Alburex® 25

Alburex® 25, 250 g/L Albumin (Human) is a ready-to-use solution and should be administered by the intravenous route only. Alburex® 25 can also be diluted in an isotonic solution of e.g. 5% glucose or 0.9% sodium chloride. 200 mL per liter gives a solution which is mildly hypooncotic and isoosmotic with citrated plasma. Alburex® 25, Albumin (Human) solution for infusion, must not be diluted with water for injection as this may cause hemolysis in recipients.

When undiluted Alburex® 25, Albumin (Human), solution for infusion is administered in patients with normal blood volume, the infusion rate should be slow enough (1-2 mL per minute) to prevent too rapid expansion of plasma volume.

SHOCK: In the treatment of shock, the amount of albumin and duration of therapy must be based on the responsiveness of the patient as indicated by blood pressure, degree of pulmonary congestion, and hematocrit. The initial dose may be followed by additional albumin within 15-30 minutes if the response is deemed inadequate. If there is continued loss of protein, it may be desirable to give packed red blood cells.

The dose should be adjusted based on patient's body weight, severity of treated condition, and estimated fluid and protein loss as determined by monitoring hemodynamic parameters, circulating volume and plasma protein levels, to avoid complications related to potential hypervolemia.

BURNS: In the treatment of burns an optimal regimen involving use of albumin, crystalloids, electrolytes and water has not been established. Suggested therapy during the first 24 hours includes administration of large volumes of crystalloid solution to maintain an adequate plasma volume. After the first 24 hours, the ratio of albumin to crystalloid may be increased to establish and maintain a plasma albumin level of about 2.5 g/100 mL or a total serum protein level of about 5.2 g/100 mL. Duration of treatment varies depending upon the extent of protein loss through renal excretion, denuded areas of skin and decreased albumin synthesis.

HYPOPROTEINEMIA: In the treatment of hypoproteinemia, 200 to 300 mL of 250 g/L Albumin (Human) may be required to reduce edema and to bring serum protein values to normal. Since such patients usually have approximately normal blood volume, doses of more than 100 mL of 250 g/L Albumin (Human) should not be given faster than 100 mL in 30 to 45 minutes to avoid circulatory embarrassment. If slower administration is desired, the product may be diluted as described in the first paragraph under **DOSAGE AND ADMINISTRATION**.

Dosing Considerations

The dose required depends on the size of the patient, the severity of trauma or illness and on continuing fluid and protein losses. Measures of adequacy of circulating volume and not plasma albumin levels, as well as hemodynamic parameters should be used to determine the dose required.

If Albumin (Human) is to be administered, hemodynamic performance should be monitored regularly; this may include:

- arterial blood pressure and pulse rate
- central venous pressure
- pulmonary artery wedge pressure
- urine output
- electrolyte
- hematocrit/hemoglobin

Missed Dose

Not applicable.

Reconstitution:

Not applicable. Alburex® is a ready-to-use solution.

OVERDOSAGE

Hypervolemia may occur if the dosage and infusion rate are too high. At the first clinical signs of cardiovascular overload (headache, dyspnea, jugular vein congestion) or increased blood pressure, raised central venous pressure and pulmonary edema, the infusion should be stopped immediately and the patient's hemodynamic parameters carefully monitored.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

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

Pharmacodynamics

Albumin (Human) is active osmotically and is therefore important in regulating the volume of circulating blood. It is a valuable therapeutic aid for the treatment of conditions that will be benefited by its marked osmotic effect.

It is convenient to use since no cross matching is required and the absence of cellular elements removes the danger of sensitization with repeated infusions.

Pharmacokinetics

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 will alter albumin kinetics and abnormal distribution may occur in conditions such as severe burns or septic shock.

Under normal conditions, the average half-life of albumin is about 19 days. The balance between synthesis and breakdown is normally achieved by feedback regulation. Elimination is predominantly intracellular and due to liposome 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 can remain increased for some hours. However, in critically ill patients, albumin can leak out of the vascular space in substantial amounts at an unpredictable rate.

When infused intravenously, 50 mL of 250 g/L Albumin (Human) draws approximately 175 mL of additional fluid into the circulation within 15 minutes, except in the presence of marked dehydration. This extra fluid reduces hemoconcentration and blood viscosity. The degree of volume expansion is dependent on the initial blood volume. When the circulating blood volume has been depleted, the hemodilution following albumin administration persists for many hours. In individuals with normal blood volume, it usually lasts only a few hours.

Duration of Effect

Refer to the Pharmacokinetics subheading.

STORAGE AND STABILITY

Alburex® 5 and Alburex® 25, Albumin (Human), solutions for infusion, can be stored either in the refrigerator or at room temperature (at +2°C to +30°C), and should be protected from light.

Keep the container in the outer carton in order to protect from light. Do not freeze.

Shelf-life: 3 years.

The product may not be used beyond the expiration date mentioned on the container label.

SPECIAL HANDLING INSTRUCTIONS

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

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

The solution should be clear or slightly opalescent. Do not use solutions which are cloudy or have deposits. This may indicate that the protein is unstable or that the solution has become contaminated.

Since this product contains no antimicrobial preservative, it should be used immediately once the stopper has been perforated. Any unused product should be disposed of in accordance with local requirements.

It is strongly recommended that every time Alburex® 5/Alburex® 25, Albumin (Human), is administered to a patient, the name and batch number of the product be recorded in order to maintain a link between the patient and the batch of the product.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Solution for infusion

Nature and contents of container:

Alburex® 5, Albumin (Human), is provided as 5% (50 g/L) solution for infusion in 100 mL, 250 mL and 500 mL vials, glass type II (Ph.Eur.).

Alburex® 25, Albumin (Human), is provided as 25% (250 g/L) solution for infusion in 50 mL and 100 mL vials, glass type II (Ph.Eur.).

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Human albumin USP

Chemical name: Serum albumin

Molecular formula and molecular mass: 66,500 Da

Structural formula: Single polypeptide chain consisting of 585 amino acids and 7 disulfide bridges. Characteristic features are a single tryptophan residue, a relatively low content of methionine (6 residues), and a large number of cystein (17) and charged amino acid residues of aspartic acid (36), glutamic acid (61), lysine (59), and arginine (23). Human albumin has a secondary structure that is about 55% α-helix. The remaining 45% is believed to be divided among turns, disordered, and β structures. Human albumin does not contain carbohydrate constituents.

Physicochemical properties: Albumin is the most abundant plasma protein comprising about 50% of the total plasma protein in humans. Each albumin molecule can bind up to 10 molecules of free fatty acid, although the actual amount bound is usually far lower.

Albumin has a pH of 6.7-7.3 for a 1% w/v solution, in 0.9% w/v NaCl solution at 20°C. A 4-5% w/v aqueous solution is isoosmotic with serum. Albumin is freely soluble in dilute salt solutions and water. Aqueous solutions containing 40% w/v albumin can be readily prepared at pH 7.4. The high net charge of the peptide contributes to its solubility in aqueous media. The seven disulfide bridges contribute to its chemical and spatial conformation. At physiological pH, albumin has a net electrostatic charge of about -17. Aqueous albumin solutions are slightly viscous and range in color from almost colorless to amber depending on the protein concentration.

Product Characteristics

Alburex® 5 and Alburex® 25, Albumin (Human) are clear, slightly viscous liquid, almost colorless, yellow, amber, or green, sterile and non-pyrogenic solutions. The concentration of the active ingredient (albumin of human origin) is 5% (50 g/L) for Alburex® 5 and 25% (250 g/L) for Alburex® 25. At least 96% of the total protein is albumin. The product contains aggregates (≤ 10.0% for Alburex® 5 and ≤ 10.0% for Alburex® 25) and trace amounts of immunoglobulins. The pH value of the ready-to-use solution is within the range of 6.4 to 7.4 for both Alburex® 5 and Alburex® 25.

Excipients: Sodium N-acetyltryptophanate and sodium caprylate are included as stabilizers, and sodium chloride is included as a tonicity agent. The solution may contain hydrochloric acid or sodium hydroxide as buffering agents. Alburex® 5 and Alburex® 25 do not contain any preservatives.

The aluminum content of Alburex® is below 200 mcg/L, which respects current European Pharmacopoeia requirements.

Viral Inactivation

The process steps that contribute to the viral safety include (1) isolation of Filtrate a, (2) isolation of Filtrate IV, (3) isolation of Filtrate d and (4) pasteurization. Validation of the above process steps through viral reduction/inactivation studies has demonstrated a significant reduction of potential viral load.

CLINICAL TRIALS

Not applicable. See ADVERSE REACTIONS section.

DETAILED PHARMACOLOGY

Human albumin is a normal constituent of human plasma and acts like physiological albumin.

MICROBIOLOGY

Not Applicable.

TOXICOLOGY

In animals, single dose toxicity testing is of little relevance and does not permit the evaluation of toxic or lethal doses or of a dose-effect relationship. Repeated dose toxicity testing is impracticable due to the development of antibodies to heterologous protein in animal models.

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

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PART III: CONSUMER INFORMATION

Alburex® 5
Alburex® 25

Albumin (Human) USP

5% and 25% Solution for Infusion

This leaflet is part III of a three-part "Product Monograph" published when Alburex® 5 and Alburex® 25 were approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Alburex®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for/what it does:

Alburex® solutions are medications used to restore and maintain the circulating blood volume in critical clinical situations such as: shock, burns and hypoproteinemia with or without edema.

When it should not be used:

Alburex® solutions should not be used if any of the following situations apply to you:

- If you are allergic to any of the components of the product (*the following two subsections address the medication composition*);
- If you suffer from severe anemia;
- If you suffer from heart failure.

What the medicinal ingredient is:

The solutions contain either 5% or 25% protein extracted from human plasma, which is the liquid part of the blood.

Alburex® 5 contains 5% (50 g/L) of protein of which at least 96% is Albumin (Human). Alburex® 25 contains 25% (250 g/L) of protein of which at least 96% is Albumin (Human).

What the important nonmedicinal ingredients are:

Sodium N-acetyltryptophanate, Sodium caprylate, Sodium chloride, Water for injection.

For a full listing of nonmedicinal ingredients, see Part 1 of the product monograph.

What dosage form it comes in:

Alburex® 5 is provided as 5% (50 g/L) solution for infusion in 100 mL, 250 mL and 500 mL vials. Alburex® 25 is provided as 25% (250 g/L) solution for infusion in 50 mL and 100 mL vials.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Alburex® is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. Because Alburex® is made from human blood, there may be a risk of transmission of infectious agents, e.g., viruses, and theoretically, the Creutzfeldt-Jakob Disease (vCJD) agent.
- Developing allergic reactions which may include flush, hives, fever, and nausea is possible. On rare occasions these reactions may lead to shock.

BEFORE you use Alburex® talk to your doctor or pharmacist if:

- you suffer from heart problems
- you suffer from high blood pressure
- you suffer from bleeding or blood clotting disorders
- you suffer from gullet varices
- you suffer from water in your lungs
- you suffer from kidney disease
- you suffer from severe anaemia

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking other drugs. No specific interaction of human albumin with other drugs medicinal product are known. However, infusing albumin may affect the medicines that bind to albumin.

PROPER USE OF THIS MEDICATION

Alburex® solutions can be infused directly into a vein or can be first diluted in an isotonic solution. Your doctor will decide which is the correct mode of administration and how much you should be given.

The product should be warmed to room temperature before use.

The solution should be clear or slightly opalescent. Solutions which are cloudy or have deposits should not be used. This may indicate that the protein is unstable or that the solution has become infected.

Once the vial has been opened, the content should be used immediately. Any unused product should be thrown away.

Your doctor will adjust the infusion rate for your individual needs. Normally, the rate is less than 5 mL/min for Alburex® 5 and 1-2mL/min for Alburex® 25 respectively. For plasma-exchange, your doctor will adjust the infusion rate to match the removal rate.

Your doctor will determine your dose based on your size, the severity of your injury or illness and on your fluid and protein losses. To determine the dose required, your doctor may monitor your circulating volume, which may include measurement of:

- blood pressures and pulse rate
- lung artery pressure
- urine production
- presence of salt and minerals
- amount of red blood cells and red blood cell protein

If allergic reactions occur, the infusion should be stopped immediately and your doctor should treat you for these reactions. In case of shock, your doctor should treat you according to the current guidelines for the management of shock.

If large volumes of Alburex® solutions are given, your blood clotting and red blood cell levels will be tested. As needed, other blood components (blood clotting factors, salts and minerals, blood platelets and red blood cells) may be given to you. Your doctor will adjust the dose and infusion rate to avoid increasing the volume of circulating blood too much. If there is any sign that this is happening (headache, uncomfortable awareness of your breathing, strong heartbeat in the throat, increased blood pressure or water in the lungs), your doctor must immediately stop the infusion.

Alburex® contains approximately 3.2 mg sodium per ml of solution (0.14 M), which should be taken into consideration for patients on a controlled sodium diet.

Your name and the batch number will usually be recorded whenever Alburex® solutions are given to you.

If you have any questions about the dose please ask your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

If you notice any side effects not mentioned in this leaflet, please inform your doctor.

In rare cases flushing, hives, fever and sickness may occur. These reactions normally disappear quickly when the infusion rate is slowed down or the infusion is stopped. In very rare cases severe reactions such as shock may occur. If this happens, the infusion should be stopped and your doctor should treat you for shock.

An excessive increase in the volume of circulating blood may occur if the dose and infusion rate are too high. If there is any sign that this is happening (headache, uncomfortable awareness of your breathing, strong heartbeat in the throat, increased blood pressure or water in the lungs), your doctor must immediately stop the infusion and check your blood circulation.

Human blood may contain certain infective agents, such as viruses, including agents of until-now unknown nature. The risk of viral infection after receiving Alburex® solutions is however reduced by careful selection of donors, blood tests for viruses and by virus removal/inactivation procedures in the production process.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Incidence of untoward reactions is low	-	-	-
Uncommon	Shock *		√	
	Flush		√	
	Hives		√	
	Fever		√	
	Nausea		√	

* Anaphylactic reaction.

This is not a complete list of side effects. For any unexpected effects while taking Alburex® solutions, contact your doctor or pharmacist.

HOW TO STORE IT

Alburex® solutions must be kept out of reach and sight of children.

It can be stored either in the refrigerator or at room temperature (at +2°C to +30°C), and should be protected from light. Do not freeze.

It must be stored in the original container and must not be used after the expiry date on the carton.

Use only clear or slightly opalescent solutions.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect*
- Call toll-free to 1-866-234-2345;
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to1-866-678-6789, or
  - Mail to:
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

* **We recommend that CSL Behring Canada, Inc. be copied when reporting suspected side effects, at the following address:**

adversereporting@cslbehring.com

or be informed by pager
Pager Number: 1-613-783-1892

MORE INFORMATION

This document, plus the full Product Monograph, prepared for health professionals can be found at:

http://www.cslbehring.ca
or for more information you may communicate with the sponsor, CSL Behring Canada, Inc. at: 1-613-783-1892 This leaflet was prepared by CSL Behring Canada, Inc.

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