PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Alburex® 5 / Alburex® 25

Albumin (Human)

5% Solution for Intravenous Infusion

25% Solution for Intravenous Infusion

USP

Plasma Substitute/Blood Derivative

ATC code: B05AA01

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RECENT MAJOR LABEL CHANGES

Not applicable.	

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Alburex® 5 (5% Albumin [Human]) and Alburex® 25 (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.

- SHOCK: Alburex® 5 and Alburex® 25 are 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® 5 and Alburex® 25 in combination with crystalloid solutions are used to maintain adequate plasma volume and protein content.
- HYPOPROTEINEMIA with or without edema: Alburex® 5 and Alburex® 25 are 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. Alburex® 5 and Alburex® 25 are not indicated as nutrient in the treatment of chronic hypoproteinemia.

1.1 Pediatrics

Pediatrics (0 - 18 years): No clinical studies using Alburex® 5 and Alburex® 25 have been conducted in pediatric patients. Safety and effectiveness in pediatric patients have not been established in clinical trials. However, extensive experience in patients suggests that children respond to Alburex® 5 and Alburex® 25 in the same manner as adults. The dosage for children and adolescents should be adjusted to patient's individual requirements.

1.2 Geriatrics

Geriatrics (65 years and older): The dosage for geriatric patients should be adjusted to patient's individual requirements.

2 CONTRAINDICATION

- Alburex® 5 (5% Albumin [Human]) and Alburex® 25 (25% Albumin [Human]) are contraindicated in patients who are hypersensitive to human albumin or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing of ingredients, see the **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING** section.
- Alburex® 5 and Alburex® 25 are contraindicated in patients with severe anemia or cardiac failure.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- Alburex® 5 and Alburex® 25 are made from human plasma and there may be a risk of transmission of infectious agents, e.g., viruses, and theoretically, the Creutzfeldt-Jakob Disease (vCJD) agent (see section **7 WARNINGS AND PRECAUTIONS**, subsection **General**).
- Developing allergic reactions which may include flush, hives, fever, and nausea is possible. On rare occasions these reactions may lead to shock.

4 DOSAGE AND ADMINISTRATION

4.1 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 Alburex® 5 (5% Albumin [Human]) and Alburex® 25 (25% Albumin [Human]) are to be administered, hemodynamic performance should be monitored regularly; this may include:

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

4.2 Recommended Dose and Dosage Adjustment

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.

Care must be taken to ensure adequate substitution of other blood components (coagulation factors, electrolytes, platelets and erythrocytes).

Alburex® 5

- 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 Alburex® 5 as a nutrient in the treatment of chronic hypoproteinemia is not recommended. In acute hypoproteinemia, Alburex® 5 may be used in replacing the protein lost in hypoproteinemic conditions. However, if edema is present or if large amounts of albumin are lost, Alburex® 25 is preferred because of the greater amount of protein in the concentrated solution.

Alburex® 25

- 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.
- 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 Alburex® 25 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 Alburex® 25 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 subsection **4.4 Administration**.

4.3 Reconstitution

Not applicable.

4.4 Administration

Alburex® 5 and Alburex® 25 are ready-to-use solutions and should be administered by the intravenous route only. The infusion rate should normally not exceed 5 mL/min for Alburex® 5 or 1-2 mL/min for Alburex® 25.

Alburex® 5 is approximately isotonic and iso-osmotic with citrated plasma. Alburex® 5 in this concentration (5% Albumin [Human]) 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.

Alburex® 25 can be diluted in an isotonic solution 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 must not be diluted with water for injection as this may cause hemolysis in recipients. When undiluted Alburex® 25 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.

If large volumes of Alburex® 5 and Alburex® 25 are administered, the products should be warmed to room temperature before use.

Alburex® 5 and Alburex® 25 should be inspected visually prior to administration. 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 Alburex® 5 and Alburex® 25 contain no antimicrobial preservative, the products should be used immediately once the stopper has been perforated. Any unused product should be disposed of in accordance with local requirements.

4.5 Missed Dose

Not applicable.

5 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.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form/ Strength/Composition	Non-medicinal Ingredients
Intravenous	Alburex® 5: Solution for infusion 5% Albumin [human] (50 g/L)	Sodium caprylate (4 mmol/L), Sodium chloride (qs a sodium content of 140 mmol/L (3.2 mg/mL)), Sodium N-acetyltryptophanate (4 mmol/L), Water for injection (qs to 1).
	Alburex® 25: Solution for infusion/ 25% Albumin [human] (250 g/L)	Sodium caprylate (20 mmol/L), Sodium chloride (qs a sodium content of 140 mmol/L (3.2 mg/mL)), Sodium N-acetyltryptophanate (20 mmol/L), Water for injection (qs to 1).

Alburex® 5 and Alburex® 25 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 ≤0.002 M. The solution contains no preservative.

Packaging

- Alburex® 5 is provided as 5% (50 g/L) solution for infusion in 250 mL and 500 mL bottles, glass type II (Ph. Eur.).
- Alburex® 25 is provided as 25% (250 g/L) solution for infusion in 50 mL and 100 mL bottles, glass type II (Ph. Eur.).

7 WARNINGS AND PRECAUTIONS

Please see **3 SERIOUS WARNINGS AND PRECAUTIONS BOX**.

Alburex® 5 (5% Albumin [Human]) and Alburex® 25 (25% Albumin [Human]) are prepared from large pools of human plasma. Thus, there is a possibility it may contain causative agents of viral or other undetermined diseases.

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

The colloid-osmotic effect of Alburex® 25 (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.

Alburex® 25 solutions are relatively low in electrolytes compared to Alburex® 5 solutions. When albumin is given, the electrolyte status of the patient should be monitored (see section **4 DOSAGE AND ADMINISTRATION** and appropriate steps taken to restore or maintain the electrolyte balance.

Protein-containing solutions such as Alburex® 5 and Alburex® 25 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 **4 DOSAGE AND ADMINISTRATION** section for information about the recommended diluents for Alburex® 25.

Alburex® 5 and Alburex® 25 contain 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® 5 and Alburex® 25 are 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 1-866-773-7721. The physician should discuss the risks and benefits of this product with the patient.

Cardiovascular

The colloid-osmotic effect of Alburex® 25 (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® 25. 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® 5 and Alburex® 25 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.

Driving and Operating Machinery

No effects on the ability to drive and use machines have been observed. Due caution should be exercised when driving or operating a vehicle or potentially dangerous machinery.

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).

Monitoring and Laboratory Tests

Refer to the Hematologic subheading.

Reproductive Health: Female and Male Potential

It is not known whether Alburex® 5 and Alburex® 25 can affect reproduction capacity. No animal reproduction studies have been conducted with Alburex® 5 and Alburex® 25. However, human albumin is a normal constituent of human blood and harmful effects on fertility are not expected.

7.1 Special Populations

7.1.1 Pregnant Women

No animal reproduction studies have been conducted with Alburex®5 and Alburex® 25. The safety of Alburex® 5 and Alburex® 25 for use in human pregnancy has not been established in controlled clinical trials and therefore the products 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.

7.1.2 Breast-feeding

It is unknown if Alburex® 5 and Alburex® 25 are excreted in human milk. Because many drugs are excreted in human milk precaution should be exercised. 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® 5 and Alburex® 25 are not expected to present a risk to the breastfed newborn/infant.

7.1.3 Pediatrics

No clinical studies using Alburex® 5 and Alburex® 25 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® 5 and Alburex® 25 in the same manner as adults. The dosage for children and adolescents should be adjusted to patient's individual requirements.

7.1.4 Geriatrics

The dosage for geriatric patients (65 years and older) should be adjusted to patient's individual requirements.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The incidence of adverse reactions to Alburex® 5 (5% Albumin [Human]) and Alburex® 25 (25% Albumin [Human]) is low. Mild reactions such as flush, urticaria, fever and nausea occur rarely. Very rarely, severe allergic reactions such as anaphylactic shock or hypersensitivity may occur.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

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[1], 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[2], 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[3] 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.

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[1] Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomized controlled trials. *BMJ.* 317:235-240, 1998.

[2] Wilkes MM, Navickis RJ. Patient survival after human albumin administration: a meta-analysis of randomized, controlled trials. *Ann Int Med.* 135:149-164, 2001.

[3] The SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004; 350: 2247-2256.

8.5 Post-Market Adverse Reactions

The incidence of adverse reactions to Alburex® 5/Alburex® 25 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 **7 WARNINGS AND PRECAUTIONS** and **13 PHARMACEUTICAL INFORMATION**.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No specific interactions of Alburex® 5 (5% Albumin [Human]) and Alburex® 25 (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.

9.4 Drug-Drug Interactions

Alburex® 5 and Alburex® 25 must not be mixed with other medicinal products (except those mentioned in **4 DOSAGE AND ADMINISTRATION** section) including whole blood and packed red cells.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 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.

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

10.2 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.

10.3 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.

11 STORAGE, STABILITY AND DISPOSAL

Alburex® 5 (5% Albumin [Human]) and Alburex® 25 (25% Albumin [Human]) 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 to protect from light. Do not freeze.

The product may not be used beyond the expiration date printed on the outer carton and container label.

Any unused product or waste material should be disposed of in accordance with local regulations.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

PART II: SCIENTIFIC INFORMATION

13 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 cysteine (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.

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.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Not applicable.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General 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.

Carcinogenicity:

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

Genotoxicity:

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

Reproductive and Developmental Toxicology:

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

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Alburex® 5 / Alburex® 25

5% Albumin (Human) / 25% Albumin (Human)

Read this carefully before you start taking **Alburex® 5 / Alburex® 25** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Alburex® 5 / Alburex® 25**.

Serious Warnings and Precautions

- Alburex® 5 and Alburex® 25 are made from human plasma and 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.

What is Alburex® 5 / Alburex® 25 used for?

Alburex® 5 / Alburex® 25 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.

How does Alburex® 5 / Alburex® 25 work?

Alburex® 5 / Alburex® 25 contain albumin that stabilises the circulating blood volume. Albumin is a carrier of hormones, enzymes, medicines, and toxins. The albumin protein in Alburex® 5 / Alburex® 25 is isolated from human blood plasma. Therefore, the albumin works exactly as if it was your own protein.

What are the ingredients in Alburex® 5 / Alburex® 25?

Medicinal ingredients:

- Either Alburex® 5 or Alburex® 25 contains 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).

Non-medicinal ingredients:

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

*For a full listing of nonmedicinal ingredients, see **PART I: HEALTH PROFESSIONAL INFORMATION** of the product monograph.*

Alburex® 5 / Alburex® 25 comes in the following dosage forms:

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

Do not use Alburex® 5 / Alburex® 25 if:

- If you are allergic to any of albumin preparations or any of the other ingredients or component of the container of the products.
- If you suffer from severe anemia;
- If you suffer from heart failure.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Alburex® 5 / Alburex® 25. Talk about any health conditions or problems you may have, including if you:

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

Other warnings you should know about:

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.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines.

The following may interact with Alburex® 5 / Alburex® 25:

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

How to take Alburex® 5 / Alburex® 25:

- Alburex® 5 / Alburex® 25 solutions can be infused directly into a vein and Alburex® 25 can also 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 bottle has been opened, the content should be used immediately. Any unused product should be thrown away.

Usual dose:

Your doctor will adjust the infusion rate for your individual needs. Normally, the rate is less than 5 mL/min for Alburex® 5 and 1-2 mL/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.

Alburex® 5 / Alburex® 25 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® 5 / Alburex® 25 solutions are given to you.

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

Overdose:

If large volumes of Alburex® 5 / Alburex® 25 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.

If you think you, or a person you are caring for, have taken too much Alburex® 5 / Alburex® 25, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

Not applicable.

What are possible side effects from using Alburex® 5 / Alburex® 25?

These are not all the possible side effects you may have when taking Alburex® 5 / Alburex® 25. If you experience any side effects not listed here, tell your healthcare professional.

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® 5 / Alburex® 25 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 and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Shock*		√	
Flush		√	
Hives		√	
Fever		√	
Nausea		√	

* Anaphylactic reaction.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. 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

Storage:

Alburex® 5 / Alburex® 25 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.

Keep out of reach and sight of children.

If you want more information about Alburex® 5 / Alburex® 25:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website (www.cslbehring.ca), or by calling 1-866-773-7721.

This leaflet was prepared by CSL Behring Canada, Inc.

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