# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Alburex5, 50 g/l, solution for infusion

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Alburex 5 is a solution containing 50 g/l of total protein of which at least 96% is human albumin.

One vial of 100 ml contains 5 g of human albumin
One vial of 250 ml contains 12.5 g of human albumin
One vial of 500 ml contains 25 g of human albumin

Alburex 5 is mildly hypooncotic to normal plasma.

Excipient with known effect:
Alburex 5 contains approximately 3.2 mg sodium per ml of solution (140 mmol/l).

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for infusion.
A clear, slightly viscous liquid; it is almost colourless, yellow, amber or green.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Restoration and maintenance of circulating blood volume where volume deficiency has been demonstrated and use of a colloid is appropriate.

The choice of albumin rather than artificial colloid will depend on the clinical situation of the individual patient, based on official recommendations.

### 4.2 Posology and method of administration

The concentration of the albumin preparation, 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 and protein losses. Measures of adequacy of

circulating volume and not plasma albumin levels should be used to determine the dose required.

If human albumin is to be administered, haemodynamic performance should be monitored regularly; this may include:

- arterial blood pressure and pulse rate
- central venous pressure
- pulmonary artery wedge pressure
- urine output
- electrolyte
- 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
Human albumin should be administered by the intravenous route only.
The infusion rate should be adjusted according to the individual circumstances and the indication.
In plasma exchange the infusion rate should be adjusted to the rate of removal.

**4.3 Contraindications**

Hypersensitivity to albumin preparations or to any of the excipients listed in section 6.1.

**4.4 Special warnings and precautions for use**

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

Albumin should be used with caution in conditions where hypervolaemia and its consequences or haemodilution could represent a special risk for the patient.
Examples of such conditions are:
· decompensated cardiac insufficiency
· hypertension
· oesophageal varices
· pulmonary oedema
· haemorrhagic diathesis
· severe anaemia
· renal and post-renal anuria

200–250 g/l human albumin solutions are relatively low in electrolytes compared to the 40–50 g/l human albumin solutions. When albumin is given, the electrolyte status of the patient should be monitored (see section 4.2) and appropriate steps taken to restore or maintain the electrolyte balance.

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 increased blood pressure, raised venous pressure and pulmonary oedema, the infusion is to be stopped immediately.

Alburex 5 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.

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.
There are no reports of virus transmissions with albumin manufactured to European Pharmacopoeia specifications by established processes.

It is strongly recommended that every time that Alburex 5 is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

## 4.5 Interaction with other medicinal products and other forms of interactions

No specific interactions of human albumin with other medicinal products are known.

## 4.6 Fertility, pregnancy and lactation

Pregnancy
No animal reproduction studies have been conducted with Alburex 5.
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 albumin suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected.

Breast-feeding
It is unknown whether Alburex 5 is excreted in human milk. Since human albumin is a normal constituent of human blood, treatment of the nursing mother with Alburex 5 is not expected to present a risk to the breastfed newborn/infant.

Fertility
No animal reproduction studies have been conducted with Alburex 5. However, human albumin is a normal constituent of human blood and harmful effects on fertility are not expected.

## 4.7 Effects on ability to drive and use machines

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

## 4.8 Undesirable effects

Summary of the safety profile
Mild reactions with human albumin solutions 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. 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.

Tabulated list of adverse reactions
The summary table below presents the adverse reactions which have been observed with Alburex during the post-marketing phase, according to the MedDRA system organ classification (SOC and Preferred Term Level).
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 reactions.
Hence the frequency category "not known (cannot be estimated from the available data)" is used.

| MedDRA System Organ Class (SOC) | Adverse Reaction | Frequency |
|---|---|---|
| Immune system disorders | Hypersensitivity reactions (including anaphylaxis and shock) | Not known |
| Gastrointestinal disorders | Nausea | Not known |
| Skin and subcutaneous tissue disorders | Flush, urticaria | Not known |

| MedDRA System Organ Class (SOC) | Adverse Reaction | Frequency |
|---|---|---|
| General disorders and administration site conditions | Fever | Not known |

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactionsvia HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; Email: medsafety@hpra.ie

For safety information with respect to transmissible agents, see section 4.4.

**4.9 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 increased blood pressure, raised central venous pressure and pulmonary oedema, the infusion should be stopped immediately and the patient's haemodynamic parameters carefully monitored.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: plasma substitutes and plasma protein fractions, ATC code: B05AA01.
Human albumin accounts quantitatively for more than half of the total protein in the plasma and represents about 10% of the protein synthesis activity of the liver.

Physico-chemical data: human albumin 50 g/l is mildly hypooncotic to normal plasma.
The most important physiological functions of albumin results from its contribution to oncotic pressure of the blood and transport function. Albumin stabilises circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.

**5.2 Pharmacokinetic properties**

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 will alter albumin kinetics and abnormal distribution may occur in conditions such as severe burns or 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 feedback regulation. Elimination is predominantly intracellular and due to lysosome 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.

### 5.3 Preclinical safety data

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

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.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Sodium N-acetyltryptophanate 4 mmol/l
Sodium caprylate 4 mmol/l
Sodium chloride q.s. to a sodium content of 140 mmol/l
Water for injections q.s. to 1 liter

### 6.2 Incompatibilities

Human albumin must not be mixed with other medicinal products, whole blood and packed red cells.

### 6.3 Shelf life

3 years.

### 6.4 Special precautions for storage

Do not store above 25 °C. Do not freeze. Keep the vial in the outer carton in order to protect from light.

### 6.5 Nature and contents of container

100 ml of solution in a single vial (glass type II) with a stopper (halogenated synthetic elastomer).
250 ml of solution in a single vial (glass type II) with a stopper ( halogenated synthetic elastomer).
500 ml of solution in a single vial (glass type II) with a stopper ( halogenated synthetic elastomer).

1 vial per pack (5 g/100 ml, 12.5 g/250 ml, 25 g/500 ml).

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

The solution can be directly administered by the intravenous route.
Albumin solutions must not be diluted with water for injections as this may cause haemolysis in recipients.
If large volumes are administered, the product should be warmed to room or body temperature before use.
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.
Once the vial has been opened, the contents should be used immediately

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

## 7 MARKETING AUTHORISATION HOLDER

CSL Behring GmbH
Emil-von-Behring-Strasse 76
35041 Marburg
Germany

## 8 MARKETING AUTHORISATION NUMBER

PA0800/008/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13th June 2014
Date of last renewal: 30th January 2019

## 10 DATE OF REVISION OF THE TEXT

September 2018