Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Albutein, 200 gram(s)/litre, solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Albutein 200 g/l is a solution containing 200 g/l (20%) of total protein of which at least 95% is human albumin.

A vial of 10 ml contains 2 g of human albumin.
A bottle of 50 ml contains 10 g of human albumin.
A bottle of 100 ml contains 20 g of human albumin.

Albutein 200 g/l has a hyperoncotic effect to normal plasma.

Excipient(s) with known effect

The solution contains between 130 - 160 mmol/l of sodium and less than 2 mmol/l of potassium.

Produced from the plasma of human donors.

For a 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.
Albutein can be used for all age groups. For paediatric population, see section 4.4.

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 safety and efficacy of Albutein 200 g/l in children have not been established in controlled clinical trials. See also section 4.4.

Method of administration

Human albumin can be directly administered by the intravenous route, or it can also be diluted in 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.

In plasma exchange the infusion-rate should be adjusted to the rate of removal.

For further details, see section 6.6.

4.3 Contraindications

Hypersensitivity to albumin preparations or to any of the excipients.

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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.

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

In a post-hoc subgroup analysis of patients with traumatic brain injury, in a randomized controlled trial of saline vs albumin as fluid resuscitation in critically ill patients, albumin was linked to increased intracranial pressure and increased mortality compared to saline solution. Albumin should therefore be used with caution in patients with traumatic brain injury.

The colloid-osmotic effect of human albumin 200 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.

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.

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

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 rate of infusion are not adjusted to the patients 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.

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 Albutein 200 g/l 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.

Paediatric population

The safety and efficacy of Albutein 200 g/l in children have not been established in controlled clinical trials.

However, clinical experience with albumin in children, suggests that no harmful effects are to be expected provided that particular attention is paid to the dose in order to avoid cardiovascular overload.

Special warnings about excipients

This medicinal product contains 33.4 mg sodium per vial of 10 ml, 166.8 mg sodium per bottle of 50 ml and 333.5 mg sodium per bottle of 100 ml, equivalent to 1.7%, 8.3% and 16.7%, respectively, of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicinal product contains potassium, less than 1 mmol (39 mg) per vial/bottle, i.e. essentially 'potassium-free'.

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

The safety of Albutein 200 g/l for use in women during pregnancy has not been established in controlled clinical trials. 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 Albutein 200 g/l is excreted into the breast milk. The excretion of human albumin into the milk has not been studied in animals. The decision whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Albutein should be made taking into account the benefit of breast-feeding for the child and the benefit of Albutein therapy for the mother.

Fertility

No animal reproduction studies have been conducted with Albutein 200 g/l.

However, human albumin is a normal constituent of human blood.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Safety profile summary

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.

Very rarely, severe reactions such as anaphylactic shock may occur. In these cases, the infusion should be stopped and an appropriate treatment should be initiated.

For safety with respect to transmissible agents, see 4.4.

Tabulated list of adverse reactions

The table presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level) and includes adverse events with the use of human albumin solutions.

There are no consistent data on the frequency of undesirable effects from clinical trials.

The following data are consistent with the safety profile of human albumin solution Grifols and confirmed post-marketing experience. Since the reporting of adverse reactions in the post-marketing is voluntary, and comes from a population of unknown size, it is not possible to reliably estimate the frequency of these reactions:

MedDRA System Organ Class (SOC)	**Adverse reaction**	**Frequency**
Immune system disorders	Anaphylactic shock Anaphylactic reaction Hypersensitivity	Unknown
Vascular disorders	Flushing	Unknown
Gastrointestinal disorders	Nausea	Unknown
Skin and subcutaneous tissue disorders	Urticaria	Unknown
General disorders and administration site conditions	Pyrexia	Unknown

Paediatric population

There are no specific data to evaluate the possibility of finding different adverse reactions in this population.

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 reactions via the national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Hypervolaemia may occur if the dosage and rate of infusion 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 200 g/l has a corresponding hyperoncotic effect.

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

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 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 cases, 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 or oncogenic or mutagenic potential.

No signs of acute toxicity have been described in animal models.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each ml contains:
Sodium chloride (q.s. sodium ion) 0.145 mmol
Sodium caprylate 0.016 mmol
Sodium N-acetyltryptophanate 0.016 mmol
Water for injections q.s.

The solution contains between 130 - 160 mmol/l of sodium and less than 2 mmol/l of potassium.

6.2 Incompatibilities

Albutein 200 g/l must not be mixed with other medicinal products (except those mentioned in section 6.6), whole blood or packed red cells.

6.3 Shelf life

3 years.
After first opening, the product should be used immediately.

6.4 Special precautions for storage

Do not store above 30 °C.
Do not freeze.
Keep the vial/bottle in the outer carton in order to protect from light.

6.5 Nature and contents of container

Albutein 200 g/l is supplied in type II glass vials/bottles, with a chlorobutyl rubber stopper, an aluminum cap, plastic top and plastic shrink band that guarantee the intactness of packaging. Vials contain 10 ml of human albumin and bottles contain 50 ml or 100 ml of human albumin.

Do not use the product if the shrink band is absent or shows any sign of tampering.

6.6 Special precautions for disposal and other handling

The solution can be directly administered by the intravenous route or it can also be diluted in an isotonic solution (e.g. 5% glucose or 0.9% sodium chloride).

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 container has been opened, the contents should be used immediately.

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

7 MARKETING AUTHORISATION HOLDER

Instituto Grifols S.A.
Polígono Levante, cl Can Guasch,2,
08150 Parets del Vallès,
Barcelona
Spain

8 MARKETING AUTHORISATION NUMBER

PA0849/006/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th October 2021

10 DATE OF REVISION OF THE TEXT