

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Albutein, 50 gram(s)/litre, solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Albutein 50 g/l is a solution containing 50 g/l (5%) of total protein of which at least 95% is human albumin.

A bottle of 100 ml contains 5 g of human albumin.

A bottle of 250 ml contains 12.5 g of human albumin.

A bottle of 500 ml contains 25 g of human albumin.

A bag of 100 ml contains 5 g of human albumin.

A bag of 250 ml contains 12.5 g of human albumin.

A bag of 500 ml contains 25 g of human albumin.

Albutein 50 g/l has a mildly hyponcotic 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 50 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.

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.

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 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 50 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 50 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 333.5 mg sodium per bottle/bag of 100 ml, 833.8 mg sodium per bottle/bag of 250 ml and 1667.5 mg sodium per bottle/bag of 500 ml, equivalent to 16.7%, 41.7% and 83.4%, 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 bottle/bag, i.e. essentially 'potassium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of Albutein 50 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 50 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 50 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 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

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 0.004 mmol

Sodium N-acetyltryptophanate 0.004 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 50 g/l must not be mixed with other medicinal products, whole blood or packed red cells.

6.3 Shelf life

Bottle: 3 years.

Bag: 2 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 bottle/bag in the outer carton in order to protect from light.

6.5 Nature and contents of container

Albutein 50 g/l can be supplied in:

- Type II glass bottles, with a chlorobutyl rubber stopper, an aluminum cap, plastic top and plastic shrink band that guarantee the intactness of packaging. Bottles contain 100 ml, 250 ml or 500 ml of human albumin.

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

- Bags (FlexBag) made of polyethylene, with a protective overwrap made of polypropylene. Bags contain 100 ml, 250 ml or 500 ml of human albumin.

Pack sizes

- 1 bottle with 100 ml, 250 ml or 500 ml per box
- 1 bag with 100 ml, 250 ml or 500 ml per box

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 container has been opened to assemble the infusion set, the contents should be used immediately.

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

Bag:

Do not remove the overwrap until ready for use. Some moisture or condensation may be observed in the protective overwrap. This is normal and does not affect the quality or safety of the albumin solution.

Check the bag for any leaks prior to use by squeezing it firmly. If leaks are detected, discard the solution.

To connect the infusion set, break the valve by twisting.

Do not use bags in series connections. Such use could result in air embolism due to residual air being drawn from the primary bag before the administration of the fluid from the secondary bag is complete.

7 MARKETING AUTHORISATION HOLDER

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Polígono Levante, cl Can Guasch,2,
08150 Parets del Vallès,
Barcelona
Spain

8 MARKETING AUTHORISATION NUMBER

PA0849/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT