Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Human Albumin Grifols 200g/l Solution for Infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human albumin

Human Albumin Grifols 200g/l is a solution containing 200 g/l of total protein of which at least 95% is human albumin.

A vial of 10 ml contains at least 1.9 g of human albumin.
A vial of 50 ml contains at least 9.5 g of human albumin.
A vial of 100 ml contains at least 19 g of human albumin.

Human Albumin Grifols 200g/l has a hyperoncotic effect.

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 safety and efficacy of Human Albumin Grifols 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.

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 listed in section 6.1.

See special warnings about excipients, section 4.4.

4.4 Special warnings and precautions for use

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. 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

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 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.

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 Human Albumin Grifols 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.

Special warning about excipients:
This medicinal product contains 1.6 mmol (36.8 mg) sodium per vial of 10 ml, 8 mmol (184 mg) sodium per vial of 50 ml, and 16 mmol (368 mg) sodium per vial of 100 ml. To be taken into consideration by patients on a controlled sodium diet.

This medicinal product contains potassium, less than 1 mmol (39 mg) per vial, 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

The safety of Human Albumin Grifols 200 g/l for use in human 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.
No animal reproduction studies have been conducted with Human Albumin Grifols 200 g/l.
Experimental animal studies are insufficient to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri- and postnatal development.

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

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 shock may occur. In these cases, the infusion should be stopped and an appropriate treatment should be initiated.

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

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517. Website: www.hpra.ie, E-mail: medsafety@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 Grifols 200g/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 bodyweight, 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 feed-back 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 the 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 chloride (q.s sodium ion)	8.48 mg/ml
Sodium caprylate	2.66 mg/ml

N-Acetyltryptophan	3.94 mg/ml
Sodium hydroxide or hydrochloric acid (for pH adjustment)	q.s.
Water for injections	q.s. to 1 ml

The solution contains between 130-160 mmol/l of sodium and not more than 2 mmol/l of potassium.

6.2 Incompatibilities

Human albumin must not be mixed with other medicinal products (except those mentioned in section 6.6), whole blood and packed red cells.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25^{o}C. Do not freeze.

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and contents of container

Type II glass infusion vial with a stopper (chlorobutyl rubber or chlorobutyl-isoprene blend rubber) which contains 10 ml, 50 ml or 100 ml of Human Albumin Grifols 200 g/l supplied in single packs.

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.

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.

Once the container 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

Instituto Grifols SA
Can Guasc
2- Parets del Valles
08150 Barcelona
Spain

8 MARKETING AUTHORISATION NUMBER

PA 0849/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization 19 October 2001
Date of last renewal 19 October 2006

10 DATE OF REVISION OF THE TEXT

May 2017