INSTRUCTIONS FOR USE

(SUMMARY OF PRODUCT CHARACTERISTICS)

1 NAME OF THE MEDICINAL PRODUCT

Albunorm 5%**,** 50 g/l, solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients:
Sodium (144-160 mmol/l)

Albunorm 5% is a mildly hypooncotic solution.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

The solution is a clear, slightly viscous liquid; it is 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

Data on the use of Albunorm 5% in children are limited; therefore, the product should only be administered to these individuals if the benefits clearly outweigh potential risks.

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.

4.3 Contraindications

Hypersensitivity to albumin preparations or to any of the excipients.

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

In a post-hoc follow-up study of critically ill patients with traumatic brain injury, fluid resuscitation with albumin was associated with higher mortality rates than was resuscitation with saline. While the mechanisms underlying this observed difference in mortality are not clear, caution is advised in the use of albumin in patients with severe traumatic brain injury.

200-250 g/l human albumin solutions are relatively low in electrolytes compared to 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.

This medicinal product contains 14.4 –16 mmol / 36-40 mmol / 72-80 mmol sodium per one bottle of 100 ml /250 ml/500 ml albumin solution, this has to be taken into consideration by patients on a controlled sodium diet.

This medicine contains maximum 1.25 mmol potassium per one bottle of 500 ml albumin solution, this has to be taken into consideration for patients with reduced kidney function or patients on a controlled potassium diet.

Standard measure 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, other pathogens and theoretically to Crutzfeld-Jacob Desease (CJD) agents.

Albumin is a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also considered extremely remote.

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 Albunorm 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 Interactions 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

The safety of Albunorm 5% 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 fetus and the neonate are to be expected.

No animal reproduction studies have been conducted with Albunorm 5%.
However, human albumin is a normal constituent of human blood.

4.7 Effect 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 case of severe reactions, the infusion should be stopped and an appropriate treatment should be initiated.

The following adverse reactions have been observed for human albumin solutions during the postmarketing phase and can therefore also be expected for Albunorm 5%.

System Organ Class	Reactions (frequency not known)*
Immune system disorders	anaphylactic shock anaphylactic reaction hypersensitivity
Psychiatric disorders	confusional state
Nervous system disorders	headache
Cardiac disorders	tachycardia bradycardia
Vascular disorders	hypotension hypertension flushing
Respiratory, thoracic and mediastinal disorders	dyspnoea
Gastrointestinal disorders	nausea
Skin and subcutaneous tissue disorders	urticaria angioneurotic oedema rash erythematosus hyperhidrosis
General disorders and administration site conditions	pyrexia chills

* cannot be estimated from the available data

For safety with respect to transmissible agents, see 4.4.

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: blood 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 40 to 50 g/l is mildly hypooncotic to normal plasma.

The most important physiological function 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 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-fetal toxicity, oncogenic or mutagenic potential.

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

N-acetyl-DL-tryptophan

Caprylic acid

Water for injections

Electrolytes

Sodium

Potassium

6.2 Incompatibilities

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

6.3 Shelf life

3 years

After the vial has been opened, the content should be used immediately.

6.4 Special precautions for storage

Store at or below 30 °C.

Store in the original container in order to protect from light.

Do not freeze.

6.5 Nature and contents of container

- 100 ml of solution in infusion bottle (Ph. Eur. / USP, type II glass) with stopper (bromobutyl rubber).
- 250 ml of solution in infusion bottle (Ph. Eur. / USP, type II glass) with stopper (bromobutyl rubber).

- 500 ml of solution in infusion bottle (Ph. Eur. / USP, type II glass) with stopper (bromobutyl rubber).

Not all pack sizes may be marketed in all countries.

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 the content should be used immediately.

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

7. PRODUCT OWNER

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9. IMPORTER AND DISTRIBUTOR

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10. DATE OF REVISION OF THE TEXT

08/2016