

DATA SHEET

OCTALBIN 5%

NAME OF THE MEDICINE

OCTALBIN 5%, Human Albumin 50 g/L, Solution for intravenous Infusion

DESCRIPTION

OCTALBIN 5% is a sterile solution of 50 mg/mL of protein of which at least 96% is human albumin. OCTALBIN 5% is a mildly hypooncotic solution.

The composition of OCTALBIN is as follows:

Component	Quantity/L
Plasma protein with at least 96% human albumin	50 g
Sodium	142.5 – 157.5 mmol
Potassium	≤ 1.0 mmol
N-acetyl-DL-tryptophan	≤ 4.2 mmol
Caprylic acid	≤ 4.2 mmol
Water for injections	1000 mL

OCTALBIN does not contain any antimicrobial or preserving agents.

PHARMACOLOGY

Pharmacodynamic properties

Pharmacotherapeutic group: plasma substitutes and plasma protein fractions,

ATC code: B05A A01

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.

Physiochemical data:

Human albumin 50 mg/mL is mildly hypooncotic compared 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.

Pharmacokinetic properties

No pharmacokinetic studies have been performed with OCTALBIN, however, the distribution, metabolism and excretion of Albumin has been extensively discussed in the scientific literature.

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 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.

OCTALBIN is administered intravenously and therefore immediately available in the body.

CLINICAL TRIALS

No comparative clinical study with OCTALBIN 5% has been carried out. However, such data exist for a similar product, OCTALBIN 25%.

A multi-center, double-blind, parallel group study with two cohorts was conducted, comparing efficacy and safety of OCTALBIN 25% with a competitor product in preventing central volume depletion after paracentesis due to cirrhotic ascites. Cohort A received treatment with Albumin after consecutive paracentesis (multiple dose treatment), whereas cohort B received treatment with Albumin after single paracentesis (single dose treatment). In total 17 patients were enrolled (11 in cohort A, 6 in cohort B). Evaluation of efficacy was based on changes from baseline of Blood Urea Nitrogen (BUN) and serum creatinine at Day 1 in cohort A. Weight changes between Day 0, Day 1 and Day 7 were also compared. No clinically relevant differences were noted between the two treatment groups with respect to changes in BUN and creatinine levels from baseline to posttreatment. No clinically relevant changes in body weight were noted between the two treatment groups. Mean BUN and mean creatinine levels are presented in Tables 1 and 2 below.

Table 1 Results for Change from Baseline in BUN (mg/dL) – All Subjects Treated						
Paracentesis	Time	Unadjusted Means		Adjusted Difference*		
1		OCTALBIN 25%	Competitor Product	Lower 95% CI	Point Estimate	Upper 95% CI
	Day 1	-2.4	0.5	-9.8	-3.5	2.7
	Day 7	-0.4	3.0	-13.3	-6.1	1.1
Table 2 Results for Change from Baseline in Serum Creatinine (mg/dL) – All Subjects Treated						
Paracentesis	Time	Unadjusted Means		Adjusted Difference*		
1		OCTALBIN 25%	Competitor Product	Lower 95% CI	Point Estimate	Upper 95% CI
	Day 1	-0.01	-0.05	-0.14	0.02	0.18
	Day 7	0.01	-0.07	-0.24	-0.01	0.21

* - Adjusted for baseline values, volume of ascites removed, cohort, and center

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.

CONTRAINDICATIONS

- Hypersensitivity to albumin preparations or to any of the excipients

WARNINGS

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 inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood and plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses or other pathogens and theoretically to Creutzfeldt-Jacob Disease (CJD) agents. The risk of transmission of infective agents is however reduced by:

- i. selection of donors by a medical interview and screening of individual donations and plasma pool for specific markers of infection
- ii. inactivation/ removal procedures included in the production process that have been validated using model viruses/pathogens.

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

The manufacturing process for OCTALBIN has been investigated for its capacity to remove prion proteins using an experimental agent of transmissible spongiform encephalopathy (TSE), considered to be a model for the CJD and vCJD agents. The manufacturing process of OCTALBIN has been shown to decrease the amount of this experimental model agent. The TSE reduction steps include separation of Fraction I+II+III and precipitation of Fraction IV.

It is strongly recommended that every time that OCTALBIN 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.

PRECAUTIONS

If allergic or anaphylactic-type reactions occur, the infusion should be stopped immediately and appropriate treatment instituted. In case of shock, the current medical standards for shock-treatment should be observed.

OCTALBIN 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

20-25% Human albumin solutions are relatively low in electrolytes compared to the 4-5% human albumin solutions. When albumin is given, the electrolyte status of the patient should be monitored (see **DOSAGE AND ADMINISTRATION**) 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 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.

OCTALBIN 5% contains trace elements of aluminium ($\leq 200 \mu\text{g/L}$). Accumulation of aluminium in patients with chronic renal insufficiency has led to toxic manifestations such as hypercalcaemia, vitamin D-refractory, osteodystrophy, anaemia and severe progressive encephalopathy. Therefore, when large volumes of albumin are contemplated for administration to such patients, serious consideration of these potential risks relative to the anticipated benefits should be given.

Use in pregnancy and lactation

The safety of OCTALBIN for use in human pregnancy has not been established in controlled clinical trials. Although 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, OCTALBIN should be given to a pregnant woman if clearly needed.

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

Paediatric use

The safety of OCTALBIN for paediatric use has not been established in controlled clinical trials.

Interactions with other medicines

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

Effects on ability to drive or operate machinery

There is no indication that albumin may impair the ability to drive and use machines.

ADVERSE EFFECTS

Adverse reactions for OCTALBIN are rare. These reactions normally disappear rapidly when the infusion rate is slowed down or the infusion is stopped. 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 OCTALBIN during the postmarketing phase.

Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000), including isolated reports.

System Organ Class	Rare	Very rare
<i>Immune system disorders</i>	anaphylactic reaction	anaphylactic shock
<i>Psychiatric disorders</i>		confusional state
<i>Nervous system disorders</i>		headache
<i>Cardiac disorders</i>		tachycardia bradycardia
<i>Vascular disorders</i>	hypotension	hypertension flushing
<i>Respiratory, thoracic and mediastinal disorders</i>		dyspnoea
<i>Gastrointestinal disorders</i>		nausea
<i>Skin and subcutaneous tissue disorders</i>		urticaria angioneurotic oedema rash erythematous increased sweating
<i>General disorders and administration site conditions</i>		fever rigors

For information on viral safety, see **PRECAUTIONS**.

DOSAGE AND 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 patient's weight, 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

This product is suitable for premature infants and dialysis patients.

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 may be higher and should be adjusted to the rate of removal.

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 infusion container has been opened the content should be used immediately. Any unused product should be disposed of in accordance with local requirements.

Incompatibilities

OCTALBIN must not be mixed with other medicinal products, whole blood or packed red cells. It must not be administered simultaneously with other intravenous preparations in the same infusion set.

OVERDOSAGE

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.

PRESENTATION

OCTALBIN 5% is supplied in the following presentations:

- 100 mL bottle, 5 g of human albumin, supplied in packs of 1 x 100 mL and 12 x 100 mL
- 250 mL bottle, 12.5 g of human albumin, supplied in packs of 1 x 250 mL and 6 x 250 mL
- 500 mL bottle, 25 g of human albumin, supplied in packs of 1 x 500 mL and 6 x 500 mL

STORAGE CONDITIONS

Shelf life is 3 years.
Store below 25°C.
Do not freeze.
Protect from light.
Do not use after expiry date.

Medicine Classification

Prescription Medicine

NAME AND ADDRESS OF SPONSOR

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