

Albumin (Human) 25%

U.S. License No. 1646

Rx only

DESCRIPTION

Albumin (Human) 25% is a sterile, liquid preparation of albumin derived from large pools of human plasma. All units of human plasma used in the manufacture of Albumin (Human) 25% are provided by FDA approved blood establishments only.

The product is manufactured by the Cohn-Oncley cold ethanol fractionation process followed by ultra- and diafiltration. The manufacturing process includes final container pasteurisation and an additional bulk pasteurisation at $60 \pm 0.5^{\circ}\text{C}$ for 10 – 11 hours. The Albumin (Human) 25% manufacturing process provides a significant viral reduction in *in vitro* studies (table 1). These reductions are achieved through a combination of process steps including Cohn fractionation and final container pasteurisation.

Table 1: In vitro reduction factor during Albumin (Human) 25% manufacturing

Production step		In vitro reduction factor [\log_{10}]					
		Enveloped viruses			Non-enveloped viruses		
		PRV	SBV	HIV-1	REO 3	PPV	HAV
Cohn fractionation*	Precipitation of Fraction I+II+III	4.58	4.28	Not done	5.55	6.89	7.41
	Precipitation of Fraction IV	> 5.50	>6.02	>7.08	> 7.84	6.29	> 7.45
	Precipitation of Fraction V	7.71	3.55	Not done	5.35	5.76	6.19
Pasteurization final container		> 8.67	> 8.79	>7.23	5.36	3.22	2.45
Global reduction factor		> 14.17	>14.81	> 14.31	> 13.20	9.51	> 9.90

* Due to the similar mode of action of the individual process steps only precipitation of Fraction IV was used to calculate the global reduction factor.

PRV: Pseudorabies Virus
SBV: Sindbis Virus
HIV-1: Human Immunodeficiency Virus - 1
Reo 3: Reovirus Type 3
PPV: Porcine Parvovirus
HAV: Hepatitis A Virus
[6-7]

The composition of Albumin (Human) 25% is as follows:

Component	Quantity/1000 ml	
Protein, of which $\geq 96\%$ is human albumin	250	g
Sodium	130 - 160	mmol
Potassium	≤ 2	mmol
N-acetyl-DL-tryptophan	0.064 - 0.096	mmol/g protein
Caprylic acid	0.064 - 0.096	mmol/g protein
Water for Injections	ad. 1000	ml

Albumin (Human) 25% contains no preservative. Albumin (Human) 25% is a clear, slightly viscous liquid; it is almost colorless or slightly yellow or green.

Albumin (Human) 25% is heated at $60 \pm 0.5^\circ\text{C}$ for 10-11 hours. No positive assertion can be made, however, that this procedure completely destroys the causative agents of viral hepatitis. There are no known cases of viral hepatitis which have resulted from the administration of Albumin (Human) 25%.

CLINICAL PHARMACOLOGY

Albumin is responsible for 70-80% of the colloid pressure of normal plasma, thus making it useful in regulating the volume of circulatory blood. Albumin stabilises circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.[1-4]

The colloid osmotic effect of Albumin (Human) 25% is approximately 5 times its volume of human plasma. When injected intravenously it will increase the circulating plasma volume by an amount of about 3.5 times the volume infused within 15 minutes if the patient is adequately hydrated. This extra fluid reduces hemoconcentration and blood viscosity. The degree and duration of volume expansion depends upon the initial blood volume. When treating patients with diminished blood volume, the effect of infused albumin may persist for many hours. The hemodilution lasts for a shorter time when albumin is administered to individuals with normal blood volume.[5]

Albumin is distributed throughout the extracellular compartments, more than 60% of the body albumin pool is located in the extravascular fluid compartment. The total body albumin in a 70 kg man is estimated to be 350g, it has a half live of about 13-19 days with a turnover of approximately 15g per day.[2-4]

INDICATIONS AND DOSAGE

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. [8]

CONTRAINDICATIONS

Hypersensitivity to albumin preparations or to any of the excipients.

Albumin should be used with caution in conditions where hypervolemia and its consequences or hemodilution could represent a special risk for the patient. Examples of such conditions are:

- Decompensated cardiac insufficiency
- Hypertension
- Esophageal varices
- Pulmonary edema
- Hemorrhagic diathesis
- Severe anemia
- Renal and post-renal anuria

[8]

WARNINGS

Albumin (Human) 25% is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating certain viruses by pasteurization. Despite these measures, such products can still potentially transmit disease. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin. There is also the possibility that unknown infectious agents may be present in such products. ALL infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Octapharma, at 866-766-4860. The physician should discuss the risks and benefits of this product with the patient.

Do not use solutions of Albumin (Human) 25% which are cloudy or have deposits. Once the infusion container has been opened the content should be used immediately. Discard unused portion.

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

PRECAUTIONS

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 and appropriate steps taken to restore or maintain the electrolyte balance.

If comparatively large volumes are to be replaced, controls of coagulation and hematocrit are necessary. Care must be taken to ensure adequate substitution of other blood constituents (coagulation factors, electrolytes, platelets and erythrocytes).

Hypervolemia may occur if the dosage and rate of infusion are not adjusted to the patient's circulatory situation. At the first clinical signs of cardiovascular overload (headache, dyspnea, jugular vein congestion), or increased blood pressure, raised venous pressure and pulmonary edema, the infusion is to be stopped immediately. [8]

Pregnancy Category C

Animal reproduction studies have not been performed with Albumin (Human) 25%. It is also not known whether Albumin (Human) 25% can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Albumin (Human) 25% should be given to a pregnant woman only if clearly needed.

ADVERSE REACTIONS

Adverse reactions for Albumin (Human) 25% 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 human albumin during the post-marketing phase. Therefore, these reactions can also be expected for Albumin (Human) 25%.

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>		dyspnea
<i>Gastrointestinal disorders</i>		nausea
<i>Skin and subcutaneous tissue disorders</i>		urticaria angioneurotic edema rash erythematous increased sweating
<i>General disorders and administration site conditions</i>		fever rigors

DOSAGE AND ADMINISTRATION

The concentration of the albumin preparation, dosage and the infusion-rate should be adjusted to the patient's individual requirements.

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. [8]

If human albumin is to be administered, hemodynamic performance should be monitored regularly; this may include:

- arterial blood pressure and pulse rate
- central venous pressure
- pulmonary artery wedge pressure
- urine output
- electrolyte
- hematocrit/hemoglobin.

[8]

Drug interactions

Components used in the packaging of Albumin (Human) 25% are latex-free.

Administration

The solution 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.

If large volumes are administered, the product should be warmed to room temperature before use.

Parenteral drug products should be inspected visually for turbidity and discoloration prior to administration, whenever solution and container permit. Do not use if turbid and/or discoloration is observed.

Filtration of Albumin (Human) 25% is not required.

HOW SUPPLIED

Albumin (Human) 25% is supplied in 12.5 g or 25.0 g single use bottles.

<u>NDC Number</u>	<u>Size</u>	<u>Grams protein</u>
67467-643-01	50 ml	12.5
67467-643-02	100 ml	25.0

STORAGE

Albumin (Human) 25% may be stored for 36 months at +2°C to +25°C (36°F to 77°F) from the date of manufacture.

Store in the original container to protect from light.

Do not freeze.

Do not use after expiration date.

CAUTION

U.S. federal law prohibits dispensing without prescription.

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REFERENCES

1. Finlayson JS: Albumin Products. *Semin.Thromb.Hemost.* 1980;6:85-120.
2. Peters T: Serum Albumin; in Putnam FW (ed): *The Plasma Proteins. Structure, function and genetic control.* New York, Academic Press, 1975, pp 133-245.
3. Quinlan GJ, Martin GS, Evans TW: Albumin: Biochemical properties and therapeutic potential. *Hepatology* 2005;41:1211-1219.
4. Tullis JL: Albumin. 1. Background and use. *JAMA* 1977;237:355-360.
5. Janeway, C. A. "Human Serum Albumin: Historical Review" in: *Proceedings of the Workshop on Albumin.* DHEW Publication No. (NIH) 76-925. Sgouris, J. T. and René A. (eds.), Washington, D.C., U.S. Government Printing Office. 1976, pp 3-21.
6. CPMP/BWP/268/95 Note for Guidance on Virus Validation Studies: The design, contribution and interpretation of studies validating the inactivation and removal of viruses.
7. CPMP/BWP/269/95, rev.3 Note for Guidance on plasma derived medicinal products.
8. CPMP/PhVWP/BPWG/2231/99/Rev1 Core SPC for Human Albumin Solution