

Albumarc® Albumin (Human), USP, 25% Solution Albumarc® 25%

SAMPLE INSTRUCTIONS ONLY

Directions for use are provided with the product and may be frequently revised. This insert is for educational purposes only. When performing laboratory techniques or using the product in therapeutic situations, use only package insert supplied with the product.

DESCRIPTION

This product is derived from blood collected from volunteer donors.

Albumin (Human), 25% Solution, Albumarc® 25%, contains in each 100 mL, 25 g of albumin prepared from pooled human venous plasma.

This product was prepared using the Cohn cold ethanol fractionation process.^{1,2} It has been adjusted to physiological pH with sodium bicarbonate and/or sodium hydroxide and has been stabilized with sodium caprylate and sodium acetyltryptophanate. The solution contains 145 ± 15 mEq of sodium per liter. Albumin (Human), 25% Solution, Albumarc® 25%, contains no preservative and none of the coagulation factors of fresh whole blood or fresh plasma. The transparent or slightly opalescent solution may have a greenish tint or may be pale straw to amber in color.

In addition to sterilization by filtration, this product has been heated for 10 hours at 60°C in the final container. This procedure has been shown to be an effective method of inactivating hepatitis viruses in 25% solutions of albumin even when prepared from plasma known to contain transmissible hepatitis viruses.³

Albumin (Human), 25% Solution, Albumarc® 25%, **must** be administered INTRAVENOUSLY.

CLINICAL PHARMACOLOGY

Albumin is a highly soluble, ellipsoidal protein (MW 66,500), accounting for 70-80% of the colloid osmotic pressure of plasma. It is, therefore, important in regulating the volume of circulating blood.^{4,4} This solution supplies the oncotic equivalent of approximately five times its volume of human plasma. When injected intravenously, 25% albumin will draw approximately 3.5 times its volume of additional fluid into the circulation within 15 minutes, if the recipient is adequately hydrated.^{3,7} This extra fluid reduces hemoconcentration and decreases blood viscosity. The degree and duration of volume expansion depend upon the initial blood volume. When treating patients with diminished blood volume, the effect of infused albumin may persist for many hours.

Albumin is also a transport protein and binds naturally occurring, therapeutic, and toxic materials in the circulation.^{4,5}

Albumin is distributed throughout the extracellular water and 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 approximately 350 g; it has a circulating life span of 15 to 20 days, with a turnover of approximately 15 g per day.⁴

The minimum serum albumin level necessary to prevent or reverse peripheral edema is unknown. Although it undoubtedly varies from patient to patient, the range probably falls near 2.5 g per deciliter. This concentration provides a plasma oncotic pressure of 20 mm Hg (the equivalent of a total protein concentration of 5.2 g/dL).⁴

Albumin (Human), 25% Solution, Albumarc® 25%, is manufactured from human plasma by the modified Cohn-Oncley cold ethanol fractionation process, which includes a series of cold-ethanol precipitation, centrifugation and/or filtration steps followed by pasteurization of the final product at 60 ± 0.5°C for 10 – 11 hours. This process accomplishes both purification of albumin and reduction of viruses.

In vitro studies demonstrate that the manufacturing process for Albumin (Human), 25% Solution, Albumarc® 25%, provides for significant viral reduction. These viral reduction studies, summarized in Table 1, demonstrate viral clearance during the manufacturing process for Albumin (Human), 25% Solution, Albumarc® 25%, using human immunodeficiency virus, type 1 (HIV-1) both as a relevant virus in its own right and a model virus for HIV-2 and other lipid enveloped viruses; bovine viral diarrheal virus (BVD), a model for lipid enveloped RNA viruses, such as hepatitis C virus (HCV); porcine parvovirus (PPV), a model for non-lipid enveloped DNA viruses such as human parvovirus B19; hepatitis A virus (HAV), a relevant virus in its own right and a model for other non-lipid enveloped RNA viruses.

These studies indicate that specific steps in the manufacture of Albumin (Human), 25% Solution, Albumarc® 25%, are capable of eliminating/inactivating a wide range of relevant and model viruses. Since the mechanism of virus elimination/inactivation at each step is different, the overall manufacturing process of Albumin (Human), 25% Solution, Albumarc® 25%, is robust in reducing viral load.

INDICATIONS AND USAGE

1. Hypovolemia (with or without shock)

Hypovolemia is a possible indication for albumin administration. The effectiveness of 25% albumin in reversing hypovolemia depends largely upon its ability to draw interstitial fluid into the circulation. Thus, it will be maximally effective only if the patient is well hydrated.²

Generally, except where signs of overhydration and/or edema are present, the treatment of acute blood volume deficit (shock) is best achieved by the administration of 5% plasma protein solution [5% Albumin (Human); 5% Plasma Protein Fraction (Human)]⁴ or, by using 25% albumin with crystalloid solutions in an albumin-to-crystalloid volume ratio of 1:3 or 1:4.

Although crystalloid solutions or colloid-containing plasma substitutes may be used in the emergency treatment of shock, Albumin (Human), 25% Solution, Albumarc® 25%, has a longer intravascular half-life.^{4,4}

When the hypovolemia is long-standing and hypoalbuminemia exists in the presence of adequate hydration or edema, 25% albumin is preferable to 5% protein solutions.^{4,4}

When the blood volume deficit is the result of hemorrhage, replacement with compatible red blood cells or whole blood should be undertaken as quickly as possible.

2. Hypoalbuminemia

A. General

Hypoalbuminemia is another possible indication for albumin administration. Hypoalbuminemia may result from one or more of the following:³

1. **Inadequate production** (malnutrition, burns, major injury, congenital analbuminemia, liver disease, infection, malignancy, endocrine disorders).
2. **Excessive catabolism** (burns, major injury, pancreatitis, thyrotoxicosis, pemphigus, nephrosis).
3. **Loss from the body** (hemorrhage, excessive renal excretion, burn exudates, exudative enteropathy, exfoliative dermatoses).
4. **Redistribution within the body** (major surgery, cirrhosis with ascites, various inflammatory conditions).

In almost every instance, treatment of the underlying disorder and emphasis on increased nutritional replacement of amino acids and/or protein will be more likely to restore normal plasma albumin levels than will the transfusion of albumin-containing solutions.^{4,7} Whenever hypoalbuminemia results from excessive protein loss, the effect of albumin administration will be temporary unless the underlying disorder is reversed.

There are occasional patients with hypoproteinemia accompanying major infections or injuries, or severe pancreatitis, for whom reversal of the disorder cannot be accomplished quickly. In these situations, supplementation of nutritional protein intake with amino acid infusions may fail to restore serum albumin to adequate levels, and 25% albumin may be a useful therapeutic adjuvant.

B. Burns

The optimal mix of crystalloid and colloid solutions which should be administered following extensive burns remains the subject of continuing discussion. During the initial 24 hours of therapy, large volumes of crystalloids are infused to restore the depleted extracellular fluid volume. Beyond 24 hours, albumin is generally used to replace the protein loss which accompanies any severe burn.^{4,4,7}

C. Adult Respiratory Distress Syndrome (ARDS)

Several factors are usually involved in the development of ARDS.^{4,4,7} One of these is a hypoproteinemic state which may be causally related to the interstitial pulmonary edema characteristic of ARDS. Although uncertainty exists concerning the precise indications for albumin infusion in ARDS, when evidence of fluid overload in the lungs is accompanied by hypoalbuminemia, the administration of 25% albumin together with a diuretic may be of therapeutic value.⁴

D. Cirrhosis

When repeated paracenteses are being performed for ascites and the fluid is not being reabsorbed, supplementary albumin infusion may be needed.⁷

E. Nephrosis

In patients with acute nephrosis who are receiving steroids and/or diuretics, success in treatment of edema may be enhanced by raising plasma oncotic pressure through the administration of 25% albumin.^{4,4}

3. Cardiopulmonary Bypass Surgery

The administration of 25% albumin prior to or during cardiopulmonary bypass surgery has been recommended although there are no clear data indicating its advantages over crystalloid solutions. Which is the most propitious time to infuse albumin is also unclear.^{4,4,10}

4. Hemolytic Disease of the Newborn (HDN)

In view of its transport role, 25% albumin may be administered in an attempt to bind and detoxify unconjugated bilirubin circulating in infants with severe HDN, thereby lessening the risk of kernicterus.⁴

Circumstances in Which Albumin Administration is Usually Not Indicated:

The interstitial redistribution of plasma albumin which accompanies major surgery only occasionally causes clinical evidence of hypovolemia or insufficient plasma oncotic pressure. Moreover, there is no evidence that this temporary redistribution adversely affects wound healing. Therefore, the administration of 25% albumin to such post-surgical patients is not usually indicated.

The sequestration of protein-rich fluid during the course of acute inflammatory conditions (peritonitis, pancreatitis, cellulitis) rarely causes significant morbidity due to hypovolemia, and treatment with albumin is rarely indicated.

Rarely does a valid reason exist for administering albumin to treat the stabilized hypoproteinemia accompanying chronic cirrhosis, chronic nephrosis, protein-losing enteropathy, malabsorption, or pancreatic insufficiency.^{4,7} However, when a patient in this category has to cope with a superimposed acute stress (e.g., anesthesia, major infection, etc.) his hemodynamic state, oncotic deficit and fluid balance should be carefully assessed and appropriate measures taken, as indicated by the individual circumstances.⁴

There is no valid reason for the use of albumin as an intravenous nutrient.

CONTRAINDICATIONS

The history of an allergic reaction to albumin is a specific contraindication to the use of this product.

WARNINGS

There exists a risk of potentially fatal hemolysis and acute renal failure from the use of Sterile Water for Injection as a diluent for Albumin (Human), 25% Solution, Albumarc® 25%. Acceptable diluents include 0.9% Sodium Chloride or 5% Dextrose in Water.

This solution should be administered with great caution to patients with hypertension, cardiac disease, severe pulmonary infection, severe chronic anemia or, hypoalbuminemia with peripheral edema. If patients with hypertension or mild congestive failure are to be infused with concentrated albumin, the 25% solution should be diluted with 5% or 10% glucose solution to reduce the albumin concentration to 10%. This dilute solution can be administered safely at the rate of 100 mL per hour. Patients should always be carefully monitored in order to guard against the possibility of circulatory overload.

DO NOT USE IF TURBID. DO NOT BEGIN ADMINISTRATION MORE THAN 4 HOURS AFTER THE CONTAINER HAS BEEN ENTERED. DISCARD UNUSED PORTION.

Albumin (Human), 25% Solution, Albumarc® 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 and/or removing certain viruses (See DESCRIPTION). Despite these measures, such products can still potentially transmit disease. Based on effective donor screening and product manufacturing processes, albumin carries an extremely remote risk for transmission of viral diseases. 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. ALL infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other health-care provider to American Red Cross at 1-800-293-5023. The physician should discuss the risks and benefits of this product with the patient.

PRECAUTIONS

(a) General

Certain components used in the packaging of this product contain natural rubber latex.

The rise in blood pressure following 25% albumin infusion necessitates careful observation of the injured or post-operative patient in order to detect and treat severed blood vessels that may not have bled at the lower blood pressure.

The increase in blood volume which follows the administration of 25% albumin may cause a significant fall in hemoglobin concentration and red blood cell transfusion may become appropriate. Administer 25% albumin slowly (1 mL/min) to patients with normal blood volume.

(b) Laboratory Tests

Although laboratory testing is not necessary in order to monitor the treatment of shock or moderate hypoalbuminemia, when Albumin (Human), 25% Solution, Albumarc® 25%, is being administered for treatment of severe hypoproteinemia, periodic measurement of serum albumin levels is advisable.

(c) Pregnancy—Category C

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

(d) Pediatric Use

Safety of this product has been demonstrated in children. Use in children is not associated with special or specific hazards, if dose is appropriate for body weight.

ADVERSE REACTIONS

Untoward reactions to Albumin (Human), 25% Solution, Albumarc® 25%, are extremely rare, although nausea, fever, chills, or urticaria may occasionally occur. Such symptoms usually disappear when the infusion is slowed or stopped for a short period of time.

DOSAGE AND ADMINISTRATION

Albumin (Human), 25% Solution, Albumarc® 25%, must be administered INTRAVENOUSLY. It may be given without dilution, or it may be given in conjunction with, or combined with other parenteral solutions, such as whole blood, plasma, saline, glucose, or sodium lactate. The addition of one volume of albumin solution to four volumes of normal saline or 5% glucose gives a solution approximately isotonic and isosmotic with citrated plasma. Albumin solutions should not be mixed with protein hydrolysates or solutions containing alcohol.

1. Hypovolemic Shock

Although the volume of administered 25% albumin and the speed of infusion must be individualized, the initial treatment of acute hypovolemia should be in the range of 100 to 200 mL of 25% albumin (25 to 50 g) for adults or 2.5 to 5 mL of 25% albumin per kilogram body weight (0.6 to 1.2 g/kg) for children. The initial dose may be repeated after 10 to 30 minutes, if the response is not adequate. For patients with significant plasma volume deficits, albumin replacement is best administered in the form of 5% Albumin (Human).

2. Hypoproteinemia With or Without Edema

Hypoalbuminemia is usually accompanied by a hidden extravascular albumin deficiency of equal magnitude. This total body albumin deficit must be considered when determining the amount of albumin necessary to reverse the hypoproteinemia. When using the patient's serum albumin concentration to estimate albumin deficit, the body albumin space should be calculated to be 80 to 100 mL per kilogram body weight.^{4,5,7} Daily doses should not exceed 2 g of albumin per kilogram body weight.

3. Hemolytic Disease of the Newborn

Albumin (Human), 25% Solution, Albumarc® 25% may be administered to jaundiced infants prior to exchange transfusion in a dose of 1 g per kilogram body weight¹¹ and may be administered during the procedure.¹²

Preparation for Administration

1. Remove cap from bottle to expose center portion of rubber stopper.
2. Clean stopper with germicidal solution.
3. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Administration

Follow directions for use that accompany the administration set. Make certain that the administration set contains an adequate filter.

HOW SUPPLIED

Albumin (Human), 25% Solution, Albumarc® 25%, is supplied in 50 mL (12.5 g) and 100 mL (25 g) bottles.

STORAGE

Store Albumin (Human), 25% Solution, Albumarc® 25%, at room temperature, not to exceed 30°C (86°F). Avoid freezing to prevent damage to the bottle.

REFERENCES

1. Cohn EJ, Strong LE, Hughes WL, *et al*: Preparation and properties of serum and plasma proteins. IV. A system for the separation into fractions of the protein and lipoprotein components of biological tissues and fluids. *J Am Chem Soc* **68**:459-475, 1946
2. Janeway CA: Human serum albumin: Historical review, in *Proceedings of the Workshop on Albumin*. Sgouris JT and Rene A (eds), Bethesda, MD, DHEW Publication NIH 76-925, 1975, pp 3-21
3. Gellis SS, Neefe JR, Stokes J Jr, *et al*: Chemical, clinical and immunological studies on the products of human plasma fractionation. XXXVI. Inactivation of the virus of homologous serum hepatitis in solutions of normal serum albumin by means of heat. *J Clin Invest* **27**: 239-244, 1948
4. Finlayson JS: Albumin products. *Sem Thromb Hemostas* **6**: 85-120, 1980
5. Peters T Jr: Serum albumin, in *The Plasma Proteins, 2nd Edition, Vol 1*. Putnam FW (ed), New York, Academic Press, 1975, pp 133-181
6. Tullis JL: Albumin 1. Background and use. 2. Guidelines for clinical use. *JAMA* **237**: 355-360, 460-463, 1977
7. Silver H: Normal serum albumin and plasma protein fraction in **Blood, Blood Components and Derivatives in Transfusion Therapy: A Technical Workshop**. Washington, DC, American Association of Blood Banks, 1980 pp 89-95
8. Heyl JT, Gibson JG II, Janeway CA: Studies on the plasma proteins. V. The effect of concentrated solutions of human and bovine serum albumin on blood volume after acute blood loss in man. *J Clin Invest* **22**: 763-773, 1943
9. Shoemaker WC, Hauser CJ: Critique of crystalloid versus colloid therapy in shock and shock lung. *Crit Care Med* **7**: 117-124, 1979
10. Lowenstein E: Blood conservation in open heart surgery. *Cleve Clin Q* **48**: 112-125, 1981
11. Wood B, Copley A, Sherwell J: Effect of additional albumin administration during exchange transfusion on plasma albumin-binding capacity. *Arch Dis Child* **45**: 59-62, 1970
12. Sao YC, Yu YHH: Albumin in the management of neonatal hyperbilirubinemia. *Arch Dis Child* **47**: 250-256, 1972

To enroll in the confidential, industry-wide Patient Notification System, call 1-888-UPDATE U (1-888-873-2838).

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Table 1 Summary of Viral Reduction Factor for Each Virus and Processing Step					
Process Step	Viral Reduction Factor (log ₁₀)				
	Lipid Enveloped			Non-lipid Enveloped	
	BVD	HIV-1	PRV	HAV	PPV
Step 1: Processing of cryo-poor plasma to Fraction I+II+III centrifugate	1.2±0.0	5.8±0.0	4.6±0.5	1.9±0.8	1.4±0.1
Step 2: Processing of Fraction I+II+III centrifugate to Fraction IV: centrifugate	2.8±0.5	NCM	3.4±0.4	1.9±0.7	(1.2±0.3)*
Step 3: Processing of Fraction IV: centrifugate to Fraction IV: centrifugate/filter press filtrate**	>2.4±0.1/>2.4±0.1	≥4.4±0.5/≥4.5±0.5	>4.8±0.1/>4.8±0.1	3.8±0.1/2.9±0.2	2.2±0.3/2.0±0.3
Step 4: Processing of Fraction IV: centrifugate/filter press filtrate to Fraction IV: Cuno 70C filtrate†	>1.6±0.2/>1.7±0.1	NCM	>4.1±0.5/>4.4±0.1	4.7±0.1/4.6±0.1	2.3±0.3/3.0±0.8
Step 5: Processing of Fraction V suspension to Cuno 90LP filtrate	(0.2±0.2)*	≥5.0±0.5	>4.6±0.0	4.2±0.4	3.4±0.5
Step 6: Pasteurization	>4.9±0.1	>5.1±0.3	>5.3±0.1	5.3±0.4	NT
Cumulative Reduction Factor^{††}, log₁₀	>12.9/13.0	>20.3/20.4	>26.8/27.1	21.8/20.8	9.3/9.8

NT Not tested.

NCM No virus reduction claim made at this step.

* Since the reduction factor of ≤1.0 is within the variability limit of the assay, these values are not included in the computation of the cumulative reduction factor.

** Two reduction factors indicate the two liquid-solid separation options available at this step.

† Two reduction factors indicate the two starting materials at this step.

†† Two cumulative reduction factors derived from the use of the two liquid-solid separation options available at Step 3.