# Albumarc®
# Albumin (Human), USP, 5% Solution
# Albumarc® 5%

**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), 5% Solution, Albumarc® 5%, contains in each 100 mL, 5 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), 5% Solution, Albumarc® 5%, 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]

The processing of Albumin (Human), 5% Solution, Albumarc® 5%, has removed blood group isoagglutinins to permit its administration without regard to the recipient's blood group. Albumin (Human), 5% Solution, Albumarc® 5%, 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.[4,5,6] This solution supplies the oncotic equivalent of approximately its volume of normal human plasma. When injected intravenously, 5% albumin will increase the circulating plasma volume by an amount approximately equal to the volume infused. This extra fluid reduces the 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. In individuals with normal blood volumes, the hemodilution lasts for a much shorter time.

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 15-20 days, with a turnover of approximately 15 g per day.[5]

The minimum serum albumin level necessary to prevent or reverse peripheral edema is unknown. Although it undoubtedly varies from patient to patient, there is some evidence that it 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).[6,7]

Albumin (Human), 5% Solution, Albumarc® 5%, 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), 5% Solution, Albumarc® 5%, provides for significant viral reduction. These viral reduction studies, summarized in Table 1, demonstrate viral clearance during the manufacturing process for Albumin (Human), 5% Solution, Albumarc® 5%, 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 enveloped RNA 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 manufacturing steps for Albumin (Human), 5% Solution, Albumarc® 5%, 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), 5% Solution, Albumarc® 5%, 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 5% albumin in reversing hypovolemia depends largely upon its colloid osmotic pressure.

Although crystalloid solutions or colloid-containing plasma substitutes may be used in the emergency treatment of shock, Albumin (Human) has a longer intravascular half-life.[7,8,9]

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.[4,6]

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:[5]
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.[4,6] 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 5% 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.[4,7] 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 indicated to replace the protein loss which accompanies any severe burn.[4,6,7]

**C. Cirrhosis**
When repeated paracenteses are being performed for ascites and the fluid is not being reinfused, supplementary albumin infusion may be needed.[7]

**3. Miscellaneous Indications for Albumin (Human), 5% Solution, Albumarc® 5%**
**A.** The administration of 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.[4,7,10]

**B.** When large volumes of packed red blood cells have been transfused to correct blood loss, 5% albumin may be administered in order to avoid the development of hypoalbuminemia.

**Circumstances in Which Albumin Administration Is Usually Not Indicated:**
The internal 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 5% 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 hypoproteinemias accompanying chronic cirrhosis, chronic nephrosis, protein-losing enteropathy, malabsorption, or pancreatic insufficiency. [4,6,7] 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. [6,7]

**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
This solution should be administered with great caution to patients with hypertension, cardiac disease, severe pulmonary infection, or severe chronic anemia. For the treatment of patients with hypoalbuminemia accompanied by peripheral edema, 25% albumin solution should be used.

Although the volume administered and the speed of infusion should be adapted to the patient, 5% albumin solution usually can be administered safely to older children and adults 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 PARTIALLY USED BOTTLES.

**Albumin (Human), 5% Solution, Albumarc® 5%, 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 healthcare 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 5% 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 5% albumin may cause a significant fall in hemoglobin concentration and red blood cell transfusion may become appropriate.

**(b) Laboratory Tests**
Although laboratory testing is not necessary in order to monitor the treatment of shock or moderate hypoalbuminemia, when Albumin (Human), 5% Solution, Albumarc® 5%, 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), 5% Solution, Albumarc® 5%. It is not known if Albumin (Human), 5% Solution, Albumarc® 5%, can cause fetal harm when administered to a pregnant woman, or can affect reproductive capacity. Albumin (Human), 5% Solution, Albumarc® 5%, 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), 5% Solution, Albumarc® 5%, 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), 5% Solution, Albumarc® 5%, 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.

**1. Hypovolemic Shock**
Although the volume of administered 5% albumin and the rate of infusion must be individualized, the initial treatment of acute hypovolemia should be in the range of 500 to 750 mL of 5% albumin (25-37.5 g) for adults or 12 to 20 mL of 5% albumin per kilogram body weight (0.6-1.0 g/kg) for infants and children. The initial dose may be repeated after 15 to 30 minutes, if the response is not adequate.

**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 80-100 mL per kilogram body weight.[4,5,7] Daily doses should not exceed 2 g of albumin per kilogram body weight.

When hypovolemia is long-standing and hypoalbuminemia exists in the presence of adequate hydration or edema, 25% albumin is usually preferable to 5% protein.[4]

**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), 5% Solution, Albumarc® 5%, is supplied in 250 mL (12.5 g) and 500 mL (25 g) bottles.

## STORAGE
Store Albumin (Human), 5% Solution, Albumarc® 5%, at room temperature, not to exceed 30˚C (86˚F). Avoid freezing to prevent damage to the bottle. Do not use after expiration date.

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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 $IV_1$ centrifugate | 2.8±0.5 | NCM | 3.4±0.4 | 1.9±0.7 | (1.2±0.3)* |
| Step 3: Processing of Fraction $IV_1$ centrifugate to Fraction $IV_4$ 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 $IV_4$ centrifugate/ filter press filtrate to Fraction $IV_4$ 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††, $log_{10}$** | **>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.

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