BUMINATE 25%
Albumin (Human), USP, 25% Solution

Description

BUMINATE 25%, Albumin (Human), 25% Solution is a sterile, nonpyrogenic preparation of albumin in a single dosage form for intravenous administration. Each 100 mL contains 25 g of albumin and is prepared from human venous plasma using the Cohn cold ethanol fractionation process. Source material for fractionation may be obtained from another U.S. licensed manufacturer. It has been adjusted to physiological pH with sodium bicarbonate and/or sodium hydroxide and stabilized with sodium acetyltryptophanate and sodium caprylate. The sodium content is 145 ± 15 mEq/L. This solution contains no preservative and none of the coagulation factors found in fresh whole blood or plasma. BUMINATE 25%, Albumin (Human), 25% Solution is a transparent or slightly opalescent solution which may have a greenish tint or may vary from a pale straw to an amber color.

The likelihood of the presence of viable hepatitis viruses has been minimized by heating the product for 10 hours at 60°C. This procedure has been shown to be an effective method of inactivating hepatitis virus in albumin solutions even when those solutions were prepared from plasma known to be infective.[1-3]

Clinical Pharmacology

Albumin is responsible for 70-80% of the colloid osmotic pressure of normal plasma, thus making it useful in regulating the volume of circulating blood.[4-6] Albumin is also a transport protein and binds naturally occurring, therapeutic and toxic materials in the circulation.[5,6]

BUMINATE 25%, Albumin (Human), 25% Solution is osmotically equivalent to approximately five times its volume of human plasma. When injected intravenously, 25% albumin will draw about 3.5 times its volume of additional fluid into the circulation within 15 minutes, except when the patient is markedly dehydrated. This extra fluid reduces hemoconcentration and blood viscosity. The degree and duration of volume expansion depends upon the initial blood volume. With patients treated for diminished blood volume, the effect of infused albumin may persist for many hours; however, in patients with normal volume, the duration will be shorter.[7,8]

Total body albumin is estimated to be 350 g for a 70 kg man and is distributed throughout the extracellular compartments; more than 60% is located in the extravascular fluid compartment. The half-life of albumin is 15 to 20 days with a turnover of approximately 15 g per day.[5]

The minimum plasma albumin level necessary to prevent or reverse peripheral edema is unknown. Some investigators recommend that plasma albumin levels be maintained at approximately 2.5 g/dL. This concentration provides a plasma oncotic value of 20 mm Hg.[4]

BUMINATE 25%, Albumin (Human), 25% Solution 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 BUMINATE 25%, Albumin (Human), 25% Solution provides for significant viral reduction. These viral reduction studies, summarized in Table 1, demonstrate viral clearance during the manufacturing process for BUMINATE 25%, Albumin (Human), 25% Solution using human immunodeficiency virus, type 1 (HIV-1) both as a relevant virus in its own right and as 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 steps in the manufacture of BUMINATE 25%, Albumin (Human), 25% Solution 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 BUMINATE 25%, Albumin (Human), 25% Solution is robust in reducing viral load.

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.

Indications and Usage

1. Hypovolemia

Hypovolemia is a possible indication for BUMINATE 25%, Albumin (Human), 25% Solution. Its effectiveness in reversing hypovolemia depends largely upon its ability to draw interstitial fluid into the circulation. It is most effective with patients who are well hydrated.

When hypovolemia is long standing and hypoalbuminemia exists accompanied by adequate hydration or edema, 25% albumin is preferable to 5% protein solutions.[4,6] However, in the absence of adequate or excessive hydration, 5% protein solutions should be used or 25% albumin should be diluted with crystalloid.

Although crystalloid solutions and colloid-containing plasma substitutes can be used in emergency treatment of shock, Albumin (Human) has a prolonged intravascular half-life.[9] When blood volume deficit is the result of hemorrhage, compatible red blood cells or whole blood should be administered as quickly as possible.

2. Hypoalbuminemia

A. General

Hypoalbuminemia is another possible indication for use of BUMINATE 25%, Albumin (Human), 25% Solution. Hypoalbuminemia can result from one or more of the following:[5]

(1) Inadequate production (malnutrition, burns, major injury, infections, etc.)
(2) Excessive catabolism (burns, major injury, pancreatitis, etc.)
(3) Loss from the body (hemorrhage, excessive renal excretion, burn exudates, etc.)
(4) Redistribution within the body (major surgery, various inflammatory conditions, etc.)

When albumin deficit is the result of excessive protein loss, the effect of administration of albumin will be temporary unless the underlying disorder is reversed. In most cases, increased nutritional replacement of amino acids and/or protein with concurrent treatment of the underlying disorder will restore normal plasma albumin levels more effectively than albumin solutions. Occasionally hypoalbuminemia accompanying severe injuries, infections or pancreatitis cannot be quickly reversed and nutritional supplements may fail to restore serum albumin levels. In these cases, BUMINATE 25%, Albumin (Human), 25% Solution might

be a useful therapeutic adjunct.

B. Burns

An optimum regimen for the use of albumin, electrolytes and fluid in the early treatment of burns has not been established, however, in conjunction with appropriate crystalloid therapy, BUMINATE 25%, Albumin (Human), 25% Solution may be indicated for treatment of oncotic deficits after the initial 24 hour period following extensive burns and to replace the protein loss which accompanies any severe burn.[4,6]

C. Adult Respiratory Distress Syndrome (ARDS)

A characteristic of ARDS is a hypoproteinemic state which may be causally related to the interstitial pulmonary edema. Although uncertainty exists concerning the precise indication of albumin infusion in these patients, if there is a pulmonary overload accompanied by hypoalbuminemia, 25% albumin solution may have a therapeutic effect when used with a diuretic.[4]

D. Nephrosis

BUMINATE 25%, Albumin (Human), 25% Solution may be a useful aid in treating edema in patients with severe nephrosis who are receiving steroids and/or diuretics.

3. Cardiopulmonary Bypass Surgery

BUMINATE 25%, Albumin (Human), 25% Solution has been recommended prior to or during cardiopulmonary bypass surgery, although no clear data exist indicating its advantage over crystalloid solutions.[4,6,10]

4. Hemolytic Disease of the Newborn (HDN)

BUMINATE 25%, Albumin (Human), 25% Solution may be administered in an attempt to bind and detoxify unconjugated bilirubin in infants with severe HDN.

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

Contraindications

A history of allergic reactions to albumin is a specific contraindication to the use of this product. BUMINATE 25%, Albumin (Human), 25% Solution is also contraindicated in severely anemic patients and in patients with cardiac failure.

Warnings

Do not use if turbid. Do not begin administration more than 4 hours after the container has been entered. Discard unused portion.

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

BUMINATE 25%, Albumin (Human), 25% Solution 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 Baxter Healthcare Corporation at 1-800-423-2862. The physician should discuss the risks and benefits of this product with the patient.

Precautions

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

BUMINATE 25%, Albumin (Human), 25% Solution must be administered intravenously at a rate not to exceed 1mL/min to patients with normal blood volume. More rapid administration might cause circulatory overload and pulmonary edema.

A rise in blood pressure after 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 a lower blood pressure.

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

Pediatric Use
The use of BUMINATE 25%, Albumin (Human), 25% Solution in children has not been associated with any special or specific hazard, if the dose is appropriate for the child's body weight.

Adverse Reactions

Untoward reactions to BUMINATE 25%, Albumin (Human), 25% Solution 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

BUMINATE 25%, Albumin (Human), 25% Solution must be administered intravenously. This solution may be administered in conjunction with or combined with other parenterals such as whole blood, plasma, saline, glucose or sodium lactate. The addition of four volumes of normal saline or 5% glucose to 1 volume of BUMINATE 25%, Albumin (Human), 25% Solution gives a solution which is approximately isotonic and isosmotic with citrated plasma.

Albumin solutions should not be mixed with protein hydrolysates or solutions containing alcohol.

Recommended Dosages

1. Hypovolemic Shock

   The dosage of BUMINATE 25%, Albumin (Human), 25% Solution must be individualized. As a guideline, the initial treatment should be in the range of 100 to 200 mL for adults and 2.5 to 5 mL per kilogram body weight for children. This may be repeated after 15 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).

   Upon administration of additional albumin or if hemorrhage has occurred, hemodilution and a relative anemia will follow. This condition should be controlled by the supplemental administration of compatible red blood cells or compatible whole blood.

2. Burns

   The optimal therapeutic regimen for administration of crystalloid and colloid solutions after extensive burns has not been established. When BUMINATE 25%, Albumin (Human), 25% Solution is administered after the first 24 hours following burns, the dose should be determined according to the patient's condition and response to treatment.

3. Hypoalbuminemia

   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 hypoalbuminemia. When using patient's serum albumin concentration to estimate the deficit, the body albumin compartment should be calculated to be 80 to 100 mL per kg of body weight.[5,6] Daily dose should not

exceed 2 g of albumin per kilogram of body weight.

4. Hemolytic Disease of the Newborn
   BUMINATE 25%, Albumin (Human), 25% Solution may be administered prior to or during exchange transfusion in a dose of 1 g per kilogram body weight.[11]

Preparation for Administration

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

1. Remove cap from bottle to expose center portion of rubber stopper.
2. Clean stopper with germicidal solution.

Administration
Follow directions for use printed on the administration set container. Make certain that the administration set contains an adequate filter.

How Supplied

BUMINATE 25%, Albumin (Human), 25% Solution is supplied in 20 mL, 50 mL and 100 mL bottles.

Storage

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

References

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