BUMINATE 5%
Albumin (Human), USP, 5% Solution

Description

BUMINATE 5%, Albumin (Human), 5% Solution, is a sterile, nonpyrogenic preparation of albumin in a single dosage form for intravenous administration. Each 100 mL contains 5 g of albumin and was 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 has been stabilized with sodium acetyltryptophanate and sodium caprylate. The sodium content is 145 ± 15 mEq/L. The solution contains no preservative and none of the coagulation factors found in fresh whole blood or plasma. BUMINATE 5%, Albumin (Human), 5% 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 reduced 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]

BUMINATE 5%, Albumin (Human), 5% Solution, contains no blood group isoagglutinins thereby permitting its administration without regard to the recipient's blood group.

Clinical Pharmacology

Albumin is responsible for 70-80% of the colloid osmotic pressure of normal plasma, thus making it useful in regulating and increasing blood volume.[4,5,6] It is also a transport protein and binds naturally occurring, therapeutic and toxic materials in the circulation.[5,6] BUMINATE 5%, Albumin (Human), 5% Solution, is osmotically equivalent to an equal volume of normal human plasma and will increase circulating plasma volume by an amount approximately equal to the volume infused. 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 last for many hours. In patients with normal blood volumes, the hemodilution lasts for a shorter period.[7,8]

Total body albumin is estimated to be 350 g for a 70 kg man and is distributed throughout the extracellular compartments. 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 pressure value of 20 mm Hg.[4]

BUMINATE 5%, Albumin (Human), 5% Solution, is manufactured by the modified Cohn-Oncley cold ethanol fractionation process which includes a series of cold-ethanol precipitation, centrifugation and/or filtration of human plasma followed by pasteurization of the final product at 60 ± 0.5°C for 10 – 11 hours. This process accomplishes both purification of albumin and the reduction of viruses.

In vitro studies demonstrate that the manufacturing process for BUMINATE 5%, Albumin (Human), 5% Solution, provides for significant viral reduction. These viral reduction studies, summarized in Table 1, demonstrate viral clearance during the manufacturing process for BUMINATE 5%, Albumin (Human), 5% Solution, using human immunodeficiency virus, type 1 (HIV-1) both as a relevant and 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 and a model for non-lipid enveloped RNA viruses.

These studies indicate that specific manufacturing steps for BUMINATE 5%, Albumin (Human), 5% 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 5%, Albumin (Human), 5% 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 use of BUMINATE 5%, Albumin (Human), 5% Solution. Its effectiveness in reversing hypovolemia depends largely upon its colloid osmotic pressure. Although crystalloid solutions and colloid-containing plasma substitutes can be used in emergency treatment of shock, Albumin (Human) has a longer intravascular half-life than crystalloid solutions.[9]

   When the hypovolemia is long-standing and hypoalbuminemia exists accompanied by adequate hydration or edema, treatment with BUMINATE 25%, Albumin (Human), 25% Solution, is preferable.[4,6]

   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 5%, Albumin (Human), 5% 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 administration of albumin solutions. Occasionally hypoalbuminemia accompanying severe injuries, infections or severe pancreatitis cannot be quickly reversed and nutritional supplements may fail to restore adequate plasma albumin levels. In these cases, BUMINATE 5%, Albumin (Human), 5% Solution, may be useful.

   B. Burns
   In conjunction with appropriate crystalloid therapy, BUMINATE 5%, Albumin (Human), 5% Solution, may be useful for treatment of protein deficits after the initial

24-hour period following extensive burns.[4]

3. **Miscellaneous Indications**
   BUMINATE 5%, Albumin (Human), 5% Solution, may be indicated prior to or during cardiopulmonary bypass surgery, though the data do not indicate a clear-cut advantage over crystalloid solutions.[4,6,10]

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 5%, Albumin (Human), 5% 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.

BUMINATE 5%, Albumin (Human), 5% 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 5%, Albumin (Human), 5% Solution, may be given rapidly to individuals with reduced plasma volume with the following exception: if a patient has a history of cardiac or circulatory disease, BUMINATE 5%, Albumin (Human), 5% Solution, should be administered slowly (5 to 10 mL per minute) to avoid too rapid a rise in the blood pressure.

Patients should always be carefully monitored in order to guard against the possibility of circulatory overload.

When BUMINATE 5%, Albumin (Human), 5% Solution, is used following injuries or surgery, the quick rise in blood pressure which follows administration makes it necessary to monitor the patient 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 5%, Albumin (Human), 5% Solution. It is not known whether BUMINATE 5%, Albumin (Human), 5% Solution, can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. BUMINATE 5%, Albumin (Human), 5% Solution, should be given to a pregnant woman only if clearly needed.

Pediatric Use
The use of BUMINATE 5%, Albumin (Human), 5% 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 5%, Albumin (Human), 5% 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 5%, Albumin (Human), 5% Solution, must be administered intravenously. It may be administered either in conjunction with or combined with other parenterals such as whole blood, plasma, saline, glucose or sodium lactate. The volume of the total dose and the rate of infusion depends on the patient's condition and response.

Recommended Dosages

1. Hypovolemia
   Although the volume of BUMINATE 5%, Albumin (Human), 5% Solution, administered must be individualized, the initial dose should be 250 to 500 mL for older children and adults and 12 to 20 mL per kilogram of body weight for infants and young children. It may be repeated after 30 minutes intervals if the response is not adequate.

2. 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 the patient's serum albumin concentration to estimate the deficit, the body albumin

compartment should be calculated to be 80 to 100 mL per kilogram of body weight.[5,6] Daily dose should not exceed 2 g of albumin per kilogram of body weight.

3. Burns
   When BUMINATE 5%, Albumin (Human), 5% Solution, is administered after the first 24 hours following burns, an initial dose of 500 mL is recommended.

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 5%, Albumin (Human), 5% Solution, is supplied in 250 mL and 500 mL bottles.

Storage

Store BUMINATE 5%, Albumin (Human), 5% Solution, at room temperature, not to exceed 30°C (86°F). Avoid freezing to prevent damage to the bottle.

References

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