ALBUKED - albumin (human) solution
KEDRION BIOPHARMA, INC

Albumin (Human) 5%, USP
Albuked™ 5

DESCRIPTION

Albumin (Human) 5%, USP (Albuked™ 5) is made from large pools of human venous plasma by the Cohn cold ethanol fractionation process. Part of the fractionation may be performed by another licensed manufacturer. It is prepared in accordance with the applicable requirements established by the U.S. Food and Drug Administration.

Albuked 5 is a 5% sterile solution of albumin in an aqueous diluent. The preparation is stabilized with 0.004 M sodium caprylate and 0.004 M acetyltryptophan. The approximate sodium content of the product is 145 mEq/L. Albuked 5 is clear, and pale yellow to green colored. It contains no preservative. Albuked 5 must be administered intravenously.

Each vial of Albuked 5 is heat-treated at 60°C for 10 hours against the possibility of transmitting the hepatitis viruses.

Additionally, the manufacturing process was investigated for its capacity to decrease the infectivity of an experimental agent of transmissible spongiform encephalopathy (TSE), considered as a model for the variant Creutzfeldt-Jakob disease (vCJD) and Creutzfeldt-Jakob disease (CJD) agents.(8-11) The production steps from Pooled Plasma to Effluent IV-1 in the Albuked 5 manufacturing process have been shown to decrease TSE infectivity of that experimental model agent (a total of ≥7.0 logs). These studies provide reasonable assurance that low levels of vCJD/CJD agent infectivity, if present in the starting material, would be removed.

CLINICAL PHARMACOLOGY

Albuked 5 is oncotically equivalent volume for volume to normal human plasma.

When administered intravenously to an adequately hydrated subject, the oncotic (colloid osmotic) effect of Albuked 5 is to expand the circulating blood volume by an amount approximately equal to the volume infused. It is primarily used in the treatment of shock associated with hemorrhage, surgery, trauma, burns, bacteremia, renal failure, and cardiovascular collapse.(1)

Albumin is a transport protein and it may be useful in severe jaundice in hemolytic disease of the newborn.(1) This could also be of importance in acute liver failure where albumin might serve the dual role of supporting plasma oncotic pressure, as well as binding excessive plasma bilirubin.(1)

INDICATIONS AND USAGE

Emergency Treatment of Hypovolemic Shock

Albuked 5 is iso-oncotic with normal plasma and on intravenous infusion will expand the circulating blood volume by an amount approximately equal to the volume infused. In conditions associated mainly with a volume deficit, albumin is best administered as a 5% solution (Albuked 5); but where there is an oncotic deficit, Albumin (Human) 25%, USP (Albuked™ 25) may be preferred. This is also an important consideration where the treatment of the shock state has been delayed. If Albuked 25 is used, appropriate additional crystalloid should be administered.(1)

Crystalloid solutions in volumes several times greater than that of Albuked 5 may be effective in treating shock in younger individuals who have no preexisting illness at the time of the incident. Older

patients, especially those with preexisting debilitating conditions, or those in whom the shock is caused by a medical disorder, or where the state of shock has existed for some time before active therapy could be instituted, may not tolerate hypoalbuminemia as well.(1)

Removal of ascitic fluid from a patient with cirrhosis may cause changes in cardiovascular function and even result in hypovolemic shock. In such circumstances, the use of albumin infusion may be required to support the blood volume.(1)

Burn Therapy

An optimal therapeutic regimen with respect to the administration of colloids, crystalloids, and water following extensive burns has not been established. During the first 24 hours after sustaining thermal injury, large volumes of crystalloids are infused to restore the depleted extracellular fluid volume. Beyond 24 hours, albumin can be used to maintain plasma colloid osmotic pressure. Albuked 25 may be preferred for this purpose.(1)

Cardiopulmonary Bypass(1)

With the relatively small priming volume required with modern pumps, preoperative dilution of the blood using albumin and crystalloid has been shown to be safe and well-tolerated. Although the limit to which the hematocrit and plasma protein concentration can be safely lowered has not been defined, it is common practice to adjust the albumin and crystalloid pump prime to achieve a hematocrit of 20% and a plasma albumin concentration of 2.5 g per 100 mL in the patient.

Acute Liver Failure(1)

In the uncommon situation of rapid loss of liver function, with or without coma, administration of albumin may serve the double purpose of supporting the colloid osmotic pressure of the plasma as well as binding excess plasma bilirubin.

Sequestration of Protein Rich Fluids(2)

This occurs in such conditions as acute peritonitis, pancreatitis, mediastinitis, and extensive cellulitis. The magnitude of loss into the third space may require treatment of reduced volume or oncotic activity with an infusion of albumin.

Situations in Which Albumin Administration is Not Warranted(1)

In chronic nephrosis, infused albumin is promptly excreted by the kidneys with no relief of the chronic edema or effect on the underlying renal lesion. It is of occasional use in the rapid “priming” diuresis of nephrosis. Similarly, in hypoproteinemic states associated with chronic cirrhosis, malabsorption, protein losing enteropathies, pancreatic insufficiency, and undernutrition, the infusion of albumin as a source of protein nutrition is not justified.

CONTRAINDICATIONS

Certain patients, e.g., those with a history of congestive cardiac failure, renal insufficiency or stabilized chronic anemia, are at special risk of developing circulatory overload. A history of allergic reaction to albumin is a specific contraindication for usage.

WARNINGS

Albuked 5 is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, and, theoretically, the Creutzfeldt-Jakob Disease (CJD) agent that can cause disease. The theoretical risk for transmission of CJD is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin. 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. Despite these

measures, such products can still potentially transmit disease. There is also the possibility that unknown infectious agents may be present in such products. Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some viral infections, particularly hepatitis C. 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 Grifols Therapeutics Inc. [1-800-520-2807].

The physician should discuss the risks and benefits of this product with the patient, before prescribing or administering it to the patient.

Solutions which have been frozen should not be used. Do not use if turbid. Do not begin administration more than 4 hours after the container has been entered. Partially used vials must be discarded. Vials which are cracked or which have been previously entered or damaged should not be used, as this may have allowed the entry of microorganisms. Albumin (Human) 5%, USP (Albuked™ 5) contains no preservative.

PRECAUTIONS

General

Patients should always be monitored carefully in order to guard against the possibility of circulatory overload. Albuked 5 is iso-oncotic with normal plasma and will not tend to aggravate tissue dehydration. Appropriate additional crystalloids should be administered, if required by the patient, to maintain normal fluid balance.

In hemorrhage, the administration of albumin should be supplemented by the transfusion of whole blood to treat the relative anemia associated with hemodilution.(3) When circulating blood volume has been reduced, hemodilution following the administration of albumin persists for many hours. In patients with a normal blood volume, hemodilution lasts for a much shorter period.(4-6) The rapid rise in blood pressure, which may follow the administration of a colloid with positive oncotic activity, necessitates careful observation to detect and treat severed blood vessels which may not have bled at the lower blood pressure.

Drug Interactions

Albuked 5 is compatible with whole blood and packed red cells, as well as the standard carbohydrate and electrolyte solutions intended for intravenous use. It should not be mixed with protein hydrolysates, amino acid solutions nor those containing alcohol.

Pregnancy Category C

Animal reproduction studies have not been conducted with Albuked 5. It is also not known whether Albuked 5 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Albuked 5 should be given to a pregnant woman only if clearly needed.

Pediaric Use

Safety and effectiveness in the pediatric population have not been established.

ADVERSE REACTIONS

Adverse reactions to albumin are rare. Such reactions may be allergic in nature or be due to high plasma protein levels from excessive albumin administration. Allergic manifestations include urticaria, chills, fever, and changes in respiration, pulse and blood pressure.

DOSAGE AND ADMINISTRATION

Albuked 5 should always be administered by intravenous infusion. The choice between the use of Albuked 5 and Albumin (Human) 25%, USP (Albuked™ 25) depends upon whether the patient requires primarily volume (Albuked 5) or primarily colloid osmotic activity (Albuked 25). Below a serum oncotic level of 20 mm Hg (equal to a total serum protein concentration of 5.2 g per 100 mL) there is evidence which suggests that the risk of complications increases.(1) When the oncotic pressure drops below this level, the patient should be treated with Albuked 25 together with diuretics. This is especially important in high risk patients who have undergone abdominal, cardiovascular, thoracic or urologic surgery or who have acute bacteremia.

The volume administered and the speed of administration should be adapted to the response of the individual patient.

A number of factors beyond our control could reduce the efficacy of this product or even result in an ill effect following its use. These include improper storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration, and biological differences in individual patients. Because of these factors, it is important that this product be stored properly and that the directions be followed carefully during use.

Hypovolemic Shock

The volume infused should be related to the estimated volume deficit and the speed of administration adapted to the response of the patient.

In neonates or infants, Albuked 5 may be given in large amounts.(7) The recommended dose is 10 to 20 mL/kg equivalent to 0.5 to 1.0 g albumin/kg body weight.

Burns

After a burn injury (usually beyond 24 hours) there is a close correlation between the amount of albumin infused and the resultant increase in plasma colloid osmotic pressure. The aim should be to maintain the plasma albumin concentration in the region of 2.5 ± 0.5 g per 100 mL with a plasma oncotic pressure of 20 mm Hg (equivalent to a total plasma protein concentration of 5.2 g per 100 mL).(1) This is best achieved by the intravenous administration of Albuked, usually as Albuked 25. The duration of therapy is decided by the loss of protein from burned areas and in the urine. In addition, oral or parenteral feeding with amino acids should be initiated, as the long-term administration of albumin should not be considered as a source of nutrition.

Other dosage recommendations are given under the specific indications referred to above.

Preparation for Administration

Remove seal to expose stopper. Always swab stopper top immediately with suitable antiseptic prior to entering vial.

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

Only 16 gauge needles or dispensing pins should be used with 20 mL vial sizes and larger. Needles or dispensing pins should only be inserted within the stopper area delineated by the raised ring. The stopper should be penetrated perpendicular to the plane of the stopper within the ring.

HOW SUPPLIED

Albuked 5 is available in 50 mL and 250 mL rubber-stoppered vials. Each single dose vial contains albumin in the following approximate amounts:

NDC Number	Size	Grams Albumin
76125-785-05	50 mL	2.5

76125-785-25	250 mL	12.5

STORAGE

Store at room temperature not exceeding 30°C (86°F). Do not freeze. Do not use after expiration date.

CAUTION

Rx only

U.S. federal law prohibits dispensing without prescription.

REFERENCES

1. Tullis JL. Albumin. 1. Background and use. 2. Guidelines for clinical use. JAMA. 1977;237:355-60; 460-3.
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3. Heyl JT, Janeway CA. The use of human albumin in military medicine. I. The theoretical and experimental basis for its use. US Navy Med Bull. 1942;40:785-91.
4. Janeway CA, Gibson ST, Woodruff LM, Heyl JT, Bailey OT, Newhouser LR. Chemical, clinical, and immunological studies on the products of human plasma fractionation. VII. Concentrated human serum albumin. J Clin Invest. 1944;23:465-90.
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8. Stenland CJ, Lee DC, Brown P, Petteway SR Jr, Rubenstein R. Partitioning of human and sheep forms of the pathogenic prion protein during the purification of therapeutic proteins from human plasma. Transfusion. 2002;42:1497-500.
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11. Cai K, Miller JL, Stenland CJ, Gilligan KJ, Hartwell RC, Terry JC, et al. Solvent-dependent precipitation of prion protein. Biochim Biophys Acta. 2002;1597:28-35.

Manufactured by:

Grifols Therapeutics Inc.
Research Triangle Park, NC 27709 USA
U.S. License No. 1871

For:
Kedrion Biopharma, Inc.
400 Kelby Street
Fort Lee, NJ 07024

08941132
(Rev. July 2012)

PACKAGE LABEL

Albumin (Human)
5%, USP

albuked™ 5

Heated 60°C 10 hours

For Intravenous Infusion Only

This package contains: 2.5 g albumin (human) in 50 mL aqueous diluent buffered with sodium carbonate and stabilized with 0.004 M sodium caprylate and 0.004 M acetyltryptophan. Each 50 mL is osmotically equivalent to 50 mL of plasma. Approximate sodium content: 145 mEq/L. Contains no preservative.

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

The patient and physician should discuss the risks and benefits of this product.

Dosage and Administration: Read enclosed package insert.

Single Dose Vial

Store at room temperature not exceeding 30°C (86°F). Do not freeze.

If the shrink band is absent or shows any sign of tampering, do not use the product and notify Grifols Therapeutics Inc. immediately.

Not Returnable for Credit or Exchange

CAUTION: U.S. federal law prohibits dispensing without prescription.

Rx only

50 mL

NDC 76125-785-05

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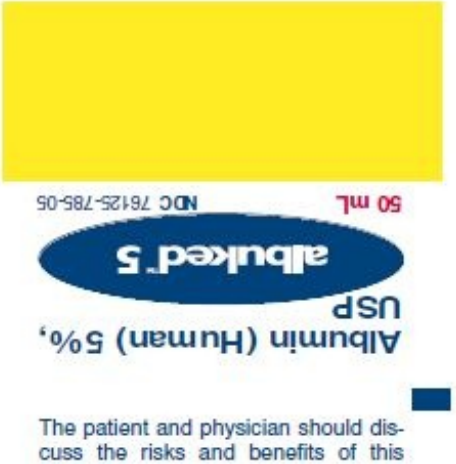
Research Triangle Park, NC 27709 USA
U.S. License No. 1871

For:
Kedrion Biopharma, Inc.
400 Kelby Street
Fort Lee, NJ 07024

Carton: 08940733



The patient and physician should discuss the risks and benefits of this product.

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Single Dose Vial

Store at room temperature not exceeding 30°C (86°F). Do not freeze.

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For:
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400 Kelby Street
Fort Lee, NJ 07024

Albumin (Human) 5%, USP

albuked™ 5

Heated 60°C 10 hours

For Intravenous Infusion Only

This package contains: 2.5 g albumin (human) in 50 mL aqueous diluent buffered with sodium carbonate and stabilized with 0.004 M sodium caprylate and 0.004 M acetyltryptophan. Each 50 mL is osmotically equivalent to 50 mL of plasma. Approximate sodium content: 145 mEq/L. Contains no preservative.

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

50 mL

NDC
76125-785-05

(01)003 76125 785055

Carton: 08940733

NDC 76125-785-06

Albumin (Human)
5%, USP

albuked™ 5

50 mL

Single Dose Vial

Manufactured by: **Grifols Therapeutics Inc.**
Research Triangle Park, NC 27709 USA
U.S. License No. 1871

For: **Kedrion Biopharma, Inc.**
400 Kelby Street, Fort Lee, NJ 07024

Rx only

The patient and physician should discuss the risks and benefits of this product.

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

For Intravenous Infusion Only

Contains 2.5 g albumin (human) in 50 mL aqueous diluent buffered with sodium carbonate and stabilized with 0.004 M sodium caprylate and 0.004 M acetyltryptophan. Each 50 mL is osmotically equivalent to 50 mL of plasma. Approximate sodium content: 145 mEq/L.

Contains no preservative. Any unused portion must be discarded.
Dosage and Administration: Read package insert.

Lot

Exp.

Mfd.

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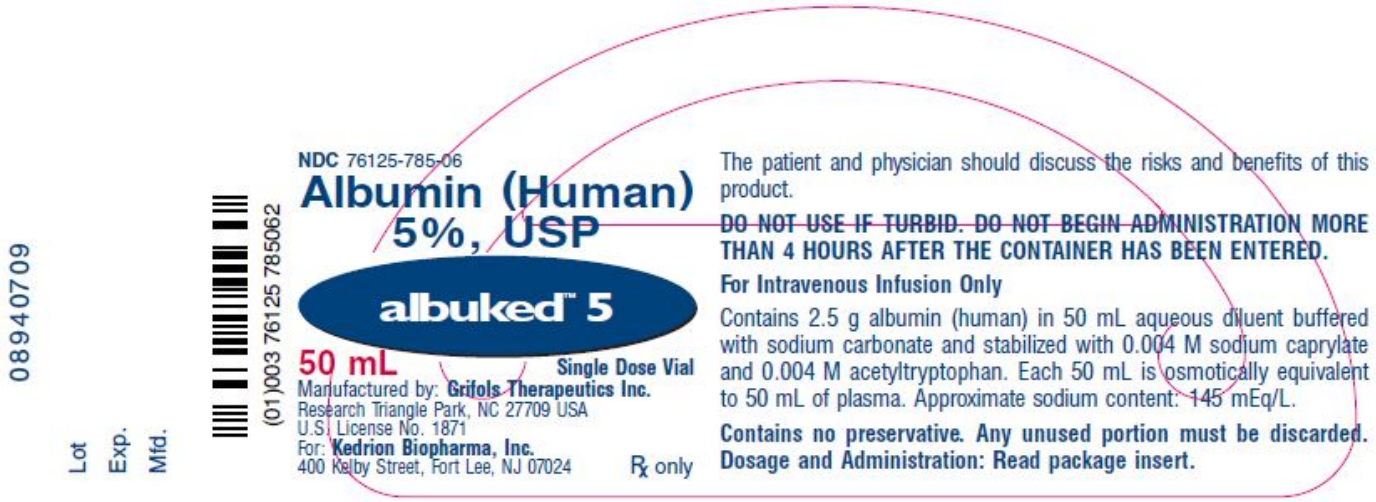

ALBUKED albumin (human) solution

Product Information

Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:76125-785
Route of Administration	INTRAVENOUS	**DEA Schedule**	

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Albumin (human) (Albumin (human))	Albumin (human)	2.5 g in 50 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-785-05	1 in 1 CARTON		
1	NDC:76125-785-06	50 mL in 1 VIAL		
2	NDC:76125-785-25	1 in 1 CARTON		
2	NDC:76125-785-26	250 mL in 1 VIAL		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101138	08/26/1976	

Labeler - KEDRION BIOPHARMA, INC (967820825)

Establishment

Name	Address	ID/FEI	Business Operations
Grifols Therapeutics Inc.		611019113	MANUFACTURE(76125-785)

Revised: 7/2012 KEDRION BIOPHARMA, INC