HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FLEXBUMIN 25% safely and effectively. See full prescribing information for FLEXBUMIN 25%.

FLEXBUMIN 25% Albumin (Human), USP, 25% Solution
For intravenous use
Initial U.S. Approval: 2005

INDICATIONS AND USAGE

FLEXBUMIN 25%, Albumin (Human) Solution is indicated for:

• Hypovolemia (1.1)
• Hypoalbuminemia: Burns, Adult Respiratory Distress Syndrome (ARDS) and Nephrosis (1.2)
• Cardiopulmonary Bypass Surgery (1.3)
• Hemolytic Disease of the Newborn (HDN) (1.4)

Limitations of Use: Albumin is not indicated as an intravenous nutrient.(1.5)

DOSAGE AND ADMINISTRATION

For intravenous use only
• Adjust dose and rate of infusion based on the patient’s clinical status. (2.1)
• Do not exceed 2 g of albumin per kg body weight for the daily dose. (2.1)
• Do not exceed 1 mL/min for patients with normal blood volume. (2.1)
• Do not dilute with Sterile Water for Injection. (2.2)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolemic Shock</td>
<td>Infants and young children: 2.5 to 5 mL per kg body weight. Older children and adults: initial dose 100 to 200 mL. Repeat after 15 to 30 minutes if the response is not adequate.</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>Calculate the body albumin compartment to be 80 to 100 mL per kg body weight. Do not exceed a daily dose of 2 g of albumin per kg of body weight.</td>
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<td>Burns:</td>
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<td>1 g per kg body weight prior to or during exchange transfusion.</td>
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1 INDICATIONS AND USAGE

FLEXBUMIN 25% [Albumin (Human)] is indicated for hypovolemia, hypoalbuminemia, cardiopulmonary bypass surgery, and hemolytic disease of the newborn (HDN).

1.1 Hypovolemia

FLEXBUMIN 25% [Albumin (Human)] is indicated for reversing hypovolemia. When hypovolemia is long standing and hypoalbuminemia exists accompanied by inadequate hydration or edema, 25% albumin should be used.11

1.2 Hypoalbuminemia

FLEXBUMIN 25% is indicated for patients with hypoalbuminemia resulting from one or more of the following:2

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

FLEXBUMIN 25% is indicated for patients with hypoalbuminemia accompanying severe infections, injuries or severe pancreatitis that cannot be quickly reversed and nutritional supplements fail to restore serum albumin levels.

1.3 Cardiopulmonary Bypass Surgery

Preoperative dilution of blood using albumin and crystalloid can be used in cardiopulmonary bypass surgery. FLEXBUMIN 25% is indicated as a component of the pump prime during cardiopulmonary bypass procedures.4,12

1.4 Hemolytic Disease of the Newborn (HDN)

FLEXBUMIN 25% is indicated for infants with severe HDN to bind and detoxify unconjugated bilirubin.

1.5 Limitations of Use

Albumin is not indicated as an intravenous nutrient.

2 DOSAGE AND ADMINISTRATION

For intravenous use only.

2.1 Dose

The dose required depends on the patient’s body weight, severity of injury/illness and on continuing fluid and protein losses. Adjust the concentration, dosage and infusion rate to the patient’s individual requirements. Use adequacy of circulating blood volume, not plasma albumin levels, to determine the dose required. Refer to Table 1 for recommended doses.

Do not exceed 2 g of albumin per kg of body weight for the daily dose. Do not exceed 1 mL/min for patients with normal blood volume. More rapid administration can cause circulatory overload and pulmonary edema.11 [See Warnings and Precautions (5.2)]

Table 1

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<th>Recommended Dose</th>
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<td>Hemolytic disease in newborn</td>
<td>1 g per kilogram body weight prior to or during exchange transfusion.</td>
</tr>
</tbody>
</table>

Hypovolemia

Reversing hypovolemia depends largely upon its ability to draw interstitial fluid into the circulation. It is most effective in patients who are well hydrated. Use 5% protein solutions or dilute 25% albumin with crystalloid solutions in the absence of adequate or excessive hydration.

Hypoalbuminemia

If albumin deficit is the result of excessive protein loss, the effect of FLEXBUMIN 25% will be temporary unless the underlying disorder is reversed.
5.3 Hemodynamics
Closely monitor hemodynamic parameters after administering FLEXBUMIN 25% for evidence of cardiac or respiratory failure, renal failure, or increasing intracranial pressure.

5.4 Blood Pressure
Monitor blood pressure in trauma patients and postoperative surgery patients resuscitated with FLEXBUMIN 25% in order to detect re-bleeding secondary to clot disruption.

5.5 Hemolysis
Do not dilute FLEXBUMIN 25% with Sterile Water for Injection as this can cause hemolysis in recipients. 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) in concentrations of 20% or higher. [See Dosage and Administration (2.2)]

5.6 Transmission of Infectious Agents
FLEXBUMIN 25% is a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD or vCJD, have ever been identified for licensed 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 US Inc. at 1-800-423-2090. The physician should discuss the risks and benefits of this product with the patient.

6 ADVERSE REACTIONS
The most serious adverse reactions are hypersensitivity reaction (including anaphylactic reaction) and pulmonary edema.

6.1 Clinical Trials Experience
No sponsor initiated clinical studies have been conducted with FLEXBUMIN 25%.

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of FLEXBUMIN 25%. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions have been reported in the post approval use of FLEXBUMIN 25%:
- Immune System Disorders: Anaphylactic shock, anaphylactic reaction, hypersensitivity/allergic reactions
- Nervous System Disorders: Headache, dysequisia
- Cardiac Disorders: Myocardial infarction, atrial fibrillation, tachycardia
- Vascular Disorders: Hypotension, flushing
- Respiratory, Thoracic, and Mediastinal Disorders: Pulmonary edema, dyspnea
- Gastrointestinal Disorders: Vomiting, nausea
- Skin and Subcutaneous Tissue Disorders: Urticaria, rash, pruritus
- General Disorders and Administration Site Conditions: Pyrexia, chills

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
No human or animal data are available to indicate the presence or absence of drug-associated risk. It is not known whether FLEXBUMIN 25% can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity.

8.2 Lactation
Risk Summary
No human or animal data are available to indicate the presence or absence of drug-associated risk. It is not known whether FLEXBUMIN 25% is excreted in human milk.

8.4 Pediatric Use
The safety of albumin solutions has been demonstrated in children provided the dose is appropriate for body weight; however, the safety of FLEXBUMIN 25% has not been evaluated in sponsor conducted pediatric studies.

8.5 Geriatric Use
No human or animal data.

10 OVERDOSE
Hypervolemia may occur if the dosage and rate of infusion are too high. [See Warnings and Precautions (5.2)]

11 DESCRIPTION
FLEXBUMIN 25% is a sterile, nonpyrogenic preparation of albumin in a single dosage form for intravenous administration. Each 100 mL contains 25 g of albumin. It has been adjusted to physiological pH with sodium bicarbonate and/or sodium hydroxide and stabilized with N-acetyltryptophan (0.02M) and sodium caprylate (0.02M). The sodium content is 145 ± 15 meq/L. FLEXBUMIN 25% contains no preservative and none of the coagulation factors found in fresh whole blood or plasma. FLEXBUMIN 25% is a transparent or slightly opalescent solution which may have a greenish tint or may vary from a pale straw to an amber color and is clear of particulate matter.

FLEXBUMIN 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 FLEXBUMIN 25% provides for effective viral reduction. These viral reduction studies, summarized in Table 2, demonstrate viral clearance during the manufacturing process for FLEXBUMIN 25%.

These studies indicate that specific steps in the manufacturing of FLEXBUMIN 25% are capable of eliminating/inactivating a wide range of relevant and model viruses. Since the mechanism of virus elimination/inactivation by fractionation and by heating steps is different, the overall manufacturing process of FLEXBUMIN 25% is effective in reducing viral load.
15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING
FLEXBUMIN 25% is supplied in a single-dose plastic container:

<table>
<thead>
<tr>
<th>NDC Number</th>
<th>Fill Size</th>
<th>Grams Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDC 0944-0493-01</td>
<td>50 mL</td>
<td>12.5 g</td>
</tr>
<tr>
<td>NDC 0944-0493-02</td>
<td>100 mL</td>
<td>25 g</td>
</tr>
</tbody>
</table>

Storage
Room temperature: not exceed 30°C (86°F). Protect from freezing.

17 PATIENT COUNSELING INFORMATION
• Inform patients of the early signs of hypersensitivity reactions, including hives, generalized urticaria, chest tightness, dyspnea, wheezing, faintness, hypotension, and anaphylaxis. [See Warnings and Precautions (5.1)]
• Inform patients that FLEXBUMIN 25% is made from human plasma and may contain infectious agents that can cause disease (e.g., viruses and, theoretically, the CJD agent). Explain that the risk of FLEXBUMIN 25% transmitting an infectious agent has been reduced by screening the plasma donors, by testing the donated plasma for certain virus infections, and by a process demonstrated to inactivate and/or remove certain viruses during manufacturing. Symptoms of a possible virus infection include headache, fever, nausea, vomiting, weakness, malaise, diarrhea, or, in the case of hepatitis, jaundice. [See Warnings and Precautions (5.6)]