INDICATIONS AND USAGE

FLEXBUM IN 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)

**Indication** | **Dose**
---|---
Hypovolemic Shock | 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.
Hypoalbuminemia | 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.
Burns | The dosage should be determined according to the patient’s condition and response to treatment after the first 24 hours.
Hemolytic Disease of the Newborn | 1 g per kg body weight prior to or during exchange transfusion. 12

ADVERSE REACTIONS

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

To report SUSPECTED ADVERSE REACTIONS, contact Baxalta US Inc., customer service at 1-800-999-1785 or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pediatric Use: Ensure dose is appropriate for body weight. (8.4)

See 17 for PATIENT COUNSELING INFORMATION

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**FULL PRESCRIBING INFORMATION**

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 adequate hydration or edema, 25% albumin should be used.4,6

1.2 Hypoalbuminemia

FLEXBUMIN 25% is indicated for patients with hypoalbuminemia resulting from one or more of the following:5

1. Adequate hydration or edema, 25% albumin should be used.4,6
2. Loss from the body (e.g., hemorrhage, excessive renal excretion, burn exudates)3
3. Redistribution within the body (e.g., major surgery, various inflammatory conditions)
4. FLEXBUMIN 25% is indicated for patients with hypoalbuminemia accompanying severe injuries, infections or severe pancreatitis that cannot be quickly reversed and nutritional supplements fail to restore serum albumin levels.

**Burns**

After the first 24 hours, FLEXBUMIN 25% is indicated, in conjunction with appropriate crystalloid therapy, for the treatment of oncotnic deficits following extensive burns and to replace protein loss which accompanies any severe burn.4,6

1.3 Cardiopulmonary Bypass Surgery

Preoperative dilution of blood using albumin and crystalloids can be used in cardiopulmonary bypass surgery. FLEXBUMIN 25% is indicated as a component of the pump priming during cardiopulmonary bypass procedures.11,12

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 **DOSE 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>
<thead>
<tr>
<th>Indication</th>
<th>Recommended 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 response is not adequate.</td>
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<td>Burns</td>
<td>The dosage should be determined according to the patient’s condition and response to treatment after the first 24 hours.</td>
</tr>
<tr>
<td>Hemolytic disease in newborn</td>
<td>1 g per kilogram body weight prior to or during exchange transfusion.12</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.

2.2 Administration

- Visually inspect parenteral drug product for particulate matter and discoloration prior to administration. 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. Do not use unless solution is clear of particulate matter or if the solution is turbid.
- Check the container for minute leaks prior to use by squeezing the bag firmly. If leaks are found, discard solution.
- Do not use the bag if the tip protector is damaged, detached or missing.
- Do not dilute with Sterile Water for Injection. Acceptable diluents include 0.9% Sodium Chloride or 5% Dextrose in Water. [See Warnings and Precautions (5.5)]
- Do not mix or add with other medicinal products including blood and blood components, protein hydrolysates or solutions containing alcohol. Do not add supplementary medication.
- Administer within 4 hours after the container has been entered.
- Monitor hemodynamic parameters in patients receiving FLEXBUMIN 25% and check for the risk of hypervolemia and cardiovascular overload. [See Warnings and Precautions (5.2)]
- Record the name and batch number of the product to maintain a link between the patient and the product.
- Discard unused portion.

CAUTION: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of fluid from the secondary container is complete.

1. Suspend container from eyelet support.
2. Remove plastic protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying the administration set.

3 **DOSE FORMS AND STRENGTHS**

FLEXBUMIN 25% is a solution containing 25 g of albumin per 100 mL.

4 **CONTRAINDICATIONS**

- Patients with a history of hypersensitivity reaction to albumin preparations or to any of the excipients (N-acetyltryptophan and sodium caprylate). Reactions have included anaphylactic shock, anaphylactic reaction, or hypersensitivity/allergic reactions. [See Warnings and Precautions (5.1) and Adverse Reactions (6.2)]
- Patients with severe anemia or cardiac failure with normal or increased intravascular volume. [See Warnings and Precautions (5.2)]

5 **WARNINGS AND PRECAUTIONS**

5.1 Hypersensitivity Reactions

Hypersensitivity reactions (including anaphylactic reactions) have been observed. Discontinue administration immediately if a hypersensitivity reaction (including anaphylactic type reactions) is suspected. In case of shock, implement standard medical treatment for shock.

5.2 Hypervolemia/Hemodilution

Under conditions where hypervolemia and/or hemodilution may occur, adjust dose and rate of infusion to the patient’s volume status. Monitor coagulation and hematologic parameters when comparatively large volumes are replaced. Ensure adequate substitution of other blood constituents (coagulation factors, platelets, and erythrocytes). Monitor electrolyte status to maintain the electrolyte balance. Discontinue administration at the first clinical signs of cardiovascular overload (e.g., headache, dyspnea, jugular venous distention, rales and abnormal elevations in systemic or central venous blood pressure). Conditions that pose increased risk of hypervolemia and/or hemodilution include but are not limited to:

- Heart failure
- Hypertension
- Esophageal varices
- Pulmonary edema
- Hemorrhagic diathesis
- Severe anemia
- Renal failure

- **Esophageal varices**
- **Pulmonary edema**
- **Hemorrhagic diathesis**
- **Severe anemia**
- **Renal failure**
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 it is not known if this risk actually exists. The risk of transmission of CJD would 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 1-800-423-2900. 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, dysgeusia
- 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 OVERDOSAGE
Hypervolemia may occur if the dosage and rate of infusion are too high. [See Warnings and Precautions (5.2)]
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. In patients with decreased
blood volume, the effect of infused albumin can persist for many hours; however,
in patients with normal blood volume, the duration will be shorter.7,8,9

12.3 Pharmacokinetics
Total body albumin is estimated to be 350 g for a 70 kg patient, more than 60% 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.9

The minimum plasma albumin level necessary to prevent or reverse peripheral edema is unknown. It is recommended that plasma albumin levels be maintained at approximately 2.5 g/dL. This concentration provides a plasma oncotic pressure value of 20 mmHg.9

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)].