Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Flexbumin 200 g/l solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Flexbumin 200 g/lis a solution containing 200 g/l (20%) of total protein of which at least 95% is human albumin.

A bag of 100 ml contains 20 g of human albumin.
A bag of 50 ml contains 10 g of human albumin

The solution is hyperoncotic.

Excipients with known effect:
Sodium 130-160 mmol/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

A clear, slightly viscous liquid; it is almost colourless, yellow, amber or green.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Restoration and maintenance of circulating blood volume where volume deficiency has been demonstrated, and use of a colloid is appropriate.
The choice of albumin rather than artificial colloid will depend on the clinical situation of the individual patient, based on official recommendations.

4.2 Posology and method of administration

The concentration of the albumin preparation, dosage and the infusion-rate should be adjusted to the patient's individual requirements.

Posology
The dose required depends on the size of the patient, the severity of trauma or illness and on continuing fluid and protein losses. Measures of adequacy of circulating volume and not plasma albumin levels should be used to determine the dose required.

If human albumin is to be administered, haemodynamic performance should be monitored regularly; this may include:
- arterial blood pressure and pulse rate
- central venous pressure
- pulmonary artery wedge pressure (PCW-pressure)
- urine output
- electrolyte
- haematocrit/haemoglobin
- clinical signs of cardiac/respiratory failure (e.g.dyspnoea)
- clinical signs of increasing intra-cranial pressure (e.g. headache)

Paediatric population
The safety and efficacy of the use of Albumin (Human) solution in paediatric patients have not been established in company-sponsored clinical trials.

Limited data on the use of Flexbumin 200 g/l in children are available, therefore no recommendations on the posology can be made. In general, the product should only be administered to these individuals if the benefits clearly outweigh the potential risks.

Method of Administration
Flexbumin 200 g/l can be directly administered by the intravenous route, or it can also be diluted in an isotonic solution (e.g. 5% glucose or 0.9 % sodium chloride). For instructions on dilution of the medicinal product before administration, see section 6.6.

The infusion-rate should be adjusted according to the individual circumstances and the indication.
In plasma exchange the infusion-rate should be adjusted to the rate of removal.

4.3 Contraindications

Hypersensitivity to albumin preparations or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the infusion. In case of shock, standard medical treatment for shock should be implemented.

Albumin should be used with caution in conditions where hypervolaemia and its consequences or haemodilution could represent a special risk for the patient. Examples of such conditions are:

- Decompensated cardiac insufficiency
- Hypertension
- Oesophageal varices
- Pulmonary oedema
- Haemorrhagic diathesis
- Severe anaemia
- Renal and post-renal anuria

The colloid-osmotic effect of human albumin 200 g/l or 250 g/l is approximately four times that of blood plasma. Therefore, when concentrated albumin is administered, care must be taken to assure adequate hydration of the patient. Patients should be monitored carefully to guard against circulatory overload and hyperhydration.

200 g/l – 250 g/l Human albumin solutions are relatively low in electrolytes compared to the 40 – 50 g/l human albumin solutions. When albumin is given, the electrolyte status of the patient should be monitored (see section 4.2 Posology) and appropriate steps taken to restore or maintain the electrolyte balance.

Flexbumin 200g/l contains sodium
50 mL bag:
This medicinal product contains 149.5-184 mg sodium per bag, equivalent to 7.5 – 9.2 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

100 mL bag:
This medicinal product contains 299-368 mg sodium per bag, equivalent to 15-18.4 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Albumin solutions must not be diluted with water for injections as this may cause haemolysis in recipients.

If comparatively large volumes are to be replaced, controls of coagulation and haematocrit are necessary. Care must be taken to ensure adequate substitution of other blood constituents (coagulation factors, electrolytes, platelets and erythrocytes).

Hypervolaemia may occur if the dosage and rate of infusion are not adjusted to the patient's circulatory situation. At the first clinical signs of cardiovascular overload (headache, dyspnoea, jugular vein congestion), or increased blood pressure, raised venous pressure and pulmonary oedema, the infusion is to be stopped immediately.

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

There are no reports of virus transmissions with albumin manufactured to European Pharmacopoeia specifications by established processes.

It is strongly recommended that every time that Flexbumin 200 g/l is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

Paediatric population:
Limited Data on the use of Flexbumin 200 g/l in children are available. The general warnings and precautions for use also apply for the paediatric population.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies of Flexbumin 200 g/l with other medicinal products have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of Flexbumin 200 g/l for use in human pregnancy has not been established in controlled clinical trials. However, clinical experience with albumin suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected.

Breast-feeding
A decision must be made whether to discontinue breast-feeding or to abstain from Flexbumin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
The effects of human albumin on fertility have not been studied.

No animal reproduction studies have been conducted with Flexbumin 200 g/l.

Experimental animal studies are insufficient to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri- and postnatal development.

However, human albumin is a normal constituent of human blood.

4.7 Effects on ability to drive and use machines

Flexbumin 200 g/l has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
Mild reactions with human albumin solutions such as flush, urticaria, fever, and nausea occur rarely. These reactions normally disappear rapidly when the infusion rate is slowed down, or the infusion is stopped. Very rarely, severe reactions such as shock may occur. In these cases, the infusion should be stopped, and an appropriate treatment should be initiated.

Frequency has been evaluated using the following criteria: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), and very rare (<1/10,000), not known (cannot be estimated from the available data).

	Very common	Common	Uncom-mon	Rare	Very rare
Immune system disorders					anaphylactic shock
Gastrointestinal disorders				nausea	
Skin and subcutaneous tissue disorders				flushing, skin rash	
General disorders and administration site conditions				fever	

In post-marketing surveillance the following adverse events have been reported. These events are listed by MedDRA System Organ Class, then by Preferred Term in order of severity.

Immune System Disorders: Anaphylactic reactions, Hypersensitivity/Allergic reactions
Nervous System Disorders: Headache, Dysguesia
Cardiac Disorders: Myocardial infarction, Atrial fibrillation, Tachycardia
Vascular Disorders: Hypotension
Respiratory, Thoracic, and Mediastinal Disorders: Pulmonary edema, Dyspnea
Gastrointestinal Disorders: Vomiting,
Skin and Subcutaneous Tissue Disorders: Urticaria, Pruritis
General Disorders and Administration Site Conditions: Chills

There are no data available on adverse reactions from clinical trials conducted with Flexbumin (Human).

For safety information with respect to transmissible agents, see section 4.4.

Paediatric population
No specific data for the paediatric population are available.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Hypervolaemia may occur if the dosage and rate of infusion are too high. At the first clinical signs of cardiovascular overload (headache, dyspnoea, jugular vein congestion), or increased blood pressure, raised central venous pressure and pulmonary oedema, the infusion should be stopped immediately and the patient's haemodynamic parameters carefully monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: plasma substitutes and plasma protein fractions
ATC code: B05AA01.

Human albumin accounts quantitatively for more than half of the total protein in the plasma and represents about 10 % of the protein synthesis activity of the liver.

Physico-chemical data: Human albumin 200 g/l or 250 g/l has a corresponding hyperoncotic effect.

The most important physiological functions of albumin result from its contribution to the oncotic pressure of the blood and its transport function. Albumin stabilises circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.

Paediatric population
No specific data on pharmacodynamic properties in the paediatric population are available.

5.2 Pharmacokinetic properties

Under normal conditions, the total exchangeable albumin pool is 4 - 5 g/kg body weight, of which 40 to 45 % is present intravascularly and 55 to 60 % in the extravascular space. Increased capillary permeability will alter albumin kinetics and abnormal distribution may occur in conditions such as severe burns or septic shock.

Under normal conditions the average half life of albumin is about 19 days. The balance between synthesis and breakdown is normally achieved by feed-back regulation. Elimination is predominantly intracellular and due to lysosome proteases.

In healthy subjects, less than 10 % of infused albumin leaves the intravascular compartment during the first two hours following infusion. There is considerable individual variation in the effect on plasma volume. In some patients the plasma volume can remain increased for some hours. However, in critically ill patients, albumin can leak out of the vascular space in substantial amounts at an unpredictable rate.

Paediatric population
No specific data on pharmacokinetic properties in the paediatric population are available.

5.3 Preclinical safety data

Human albumin is a normal constituent of human plasma and acts like physiological albumin.

In animals, single dose toxicity testing is of little relevance and does not permit the evaluation of toxic or lethal doses or of a dose-effect relationship. Repeated dose toxicity testing is impracticable due to the development of antibodies to heterologous protein in animal models.

To date, human albumin has not been reported to be associated with embryo-foetal toxicity, oncogenic or mutagenic potential.

No signs of acute toxicity have been described in animals models.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride 4.3 g/l
Sodium caprylate 2.7 g/l
Sodium acetyltryptophanate 4.3 g/l
Water for injections

Total amount of sodium ions 130 – 160 mmol/l

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products (except those mentioned in 6.6), whole blood or packed red cells.

Further human albumin should not be mixed with protein hydrolysates (e.g. parenteral nutrition) or solutions containing alcohol since these combinations may cause the proteins to precipitate.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.
Do not freeze.
Keep the bag in the outer carton in order to protect from light.

6.5 Nature and contents of container

50 or 100 ml of solution in a polyethylene bag, with an infusion port (polyethylene).
Pack sizes:
24 x 50 ml (2 boxes of 12 or 24 single units)
12 x 100 ml (2 boxes of 6 or 12 single units)
1 x 50ml (single unit)
1 x 100ml (single unit)

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The solution can be directly administered by the intravenous route, using a disposable sterile and pyrogen-free infusion set. Before inserting the infusion set in the cap, this should be disinfected with an appropriate antiseptic. Once the infusion set is attached to the bag, the contents should be perfused immediately.

The solution can also be diluted in an isotonic solution (e.g. 5 % glucose or 0.9% sodium chloride).

Albumin solutions must not be diluted with water for injections as this may cause haemolysis in recipients.

If large volumes are administered, the product should be warmed to room or body temperature before use.

Do not use the bag if the tip protector is damaged, detached or missing.

Use only if the bag seals are intact. Discard in case of leak.

Do not use solutions which are cloudy or have deposits. This may indicate that the protein is unstable or that the solution has become contaminated.

Once the container has been opened, the contents should be used immediately. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Baxalta Innovations GmbH
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A-1221 Vienna
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8 MARKETING AUTHORISATION NUMBER

PA2004/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 13th October 2011

10 DATE OF REVISION OF THE TEXT

November 2023