HUMAN ALBUMIN 20 % BEHRING

1. NAME OF THE MEDICINAL PRODUCT

Human Albumin 20 % Behring

Solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human Albumin 20 % Behring, low salt, is a solution containing 200 g/l of total protein of which at least 96 % is human albumin.

100 ml contain at least 19.2 g of human albumin.
50 ml contain at least 9.6 g of human albumin.

The solution is hyperoncotic.

For a 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

- Hypoalbuminemia (liver cirrhosis, nephrosis)
- Toxic processes (pregnancy toxicosis, hyperbilirubinemia) ,
- Volume substitution therapy.

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
- urine output
- electrolyte
- haematocrit/haemoglobin

Method of administration
Human albumin can be administered by the intravenous route, either undiluted or after dilution in an isotonic solution (e.g. 5 % glucose or 0.9 % sodium chloride). See section 3 "Pharmaceutical Form" and 6.6 "Special precautions for disposal and other handling".

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 of the product.

4.4 Special warnings and precautions for use

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. 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 or 250 g/l is approximately four times that of blood plasma. Therefore, when highly 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 or hyperhydration.

200 – 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 method of administration") and appropriate steps taken to restore or maintain the electrolyte balance.

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 patients circulatory situation. At the first clinical signs of cardiovascular overload (headache, dyspnoea, jugular vein congestion), or increased blood pressure, raised venous pressure or pulmonary oedema, the infusion is to be stopped immediately.

Human Albumin 20 % Behring, low salt contains 125 mmol sodium per litre. To be taken into consideration by patients on a controlled sodium diet.

Virus safety
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 Human Albumin 20 % Behring, low salt, 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.

4.5 Interactions with other medicinal products and other forms of interactions

No specific interactions of human albumin with other medicinal products are known.

4.6 Pregnancy and lactation

The safety of Human Albumin 20 % Behring, low salt, 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, particularly since human albumin is a normal constituent of human blood. No animal reproduction studies have been conducted with Human Albumin 20 % Behring, low salt. 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.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

The following adverse reactions are based on post marketing experience and were observed very rarely (< 1/10,000 including reported single cases):

- General disorders and administration site conditions:
  Chills, fever, nausea, vomiting, headache, malaise and flush.
- Immune system disorders:
  Hypersensitivity reactions or allergic-anaphylactic reactions such as rash, itching, urticaria, dyspnoea, tachycardia, bradycardia, hypotension. These reactions might in single cases be reaching as far as life-threatening shock.

Mild reactions normally disappear rapidly after the infusion rate has been slowed down or the infusion stopped. In case of severe reactions (e.g. anaphylactic shock) the infusion has to be stopped immediately and appropriate treatment instituted.

For safety with respect to transmissible agents, see section 4.4 "Special warnings and precautions for use".

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

https://sideeffects.health.gov.il/
and emailed to the Registration Holder's Patient Safety Unit at: PV-IL@cslbehring.com

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 or 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, albumin

ATC code: B05A A01
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 or 250 g/l has a corresponding hyperoncotic effect.
The most important physiological functions of albumin result from its contribution to oncotic pressure of the blood and transport function. Albumin stabilises the circulating blood volume and is a carrier of hormones, enzymes, medicinal products and toxins.

5.2 Pharmacokinetic properties

Under normal conditions, the total exchangeable albumin pool is 4 - 5 g/kg body weight, of which 40 - 45 % is present intravascularly and 55 - 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 feedback regulation. Elimination is predominantly intracellular and due to lysosomal proteases.

In healthy subjects, less than 10 % of infused albumin leaves the intravascular compartment during the first 2 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.

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 animal models.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

	Amount in vial with 100 ml	**Amount in vial with 50 ml**

N^1-acetyl D/L - tryptophan	392 mg	196 mg
Chloride	max 355 mg	max 177.5 mg
Sodium	288 mg	144 mg
Caprylate	228 mg	114 mg
Potassium	max 8 mg	max 4 mg
Water for injection	Ad 100 ml	Ad 50 ml

6.2 Incompatibilities

Human Albumin 20 % Behring, low salt, must not be mixed with other medicinal products (except the recommended diluents in section 6.6 "Special precautions for disposal and other handling"), whole blood and packed red cells.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
Human Albumin 20 % Behring, low salt, must not be used after the expiry date given on the pack and container.
Once the container has been opened, the contents should be used immediately.

6.4 Special precautions for storage

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

Keep out of the reach and sight of children!

6.5 Nature and contents of container

Immediate containers
Vial of 50 ml, colourless glass (Type II Ph. Eur.), sealed with a rubber stopper, aluminium seal and plastic flip-off cap.

Vial of 100 ml, colourless glass (Type II Ph. Eur.), sealed with a rubber stopper, aluminium seal and plastic flip-off cap.

Presentations
Infusion vial with 50 ml
Infusion vial with 100 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

Method of administration
Human albumin can be administered by the intravenous route, either undiluted or after dilution 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 solutions which are cloudy or contain residues (deposits/particles). This may indicate that the protein is unstable or that the solution has become contaminated.

Once the container has been opened, the contents have to be used immediately.

7. MANUFACTURER

CSL Behring GmbH
Emil-von-Behring-Str. 76
35041 Marburg
Germany

8. REGISTRATION HOLDER

CSL BEHRING LTD.,
4 Dolev st., Ra'anana 4366204

9. REGISTRATION NUMBER

039 05 20131 00

Revised in September 2023 according to MoH guidelines.

CSL Behring