Biotest

From Nature for Life

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Albiomin®: Pureness protects.

Volume. Pureness. Natural.

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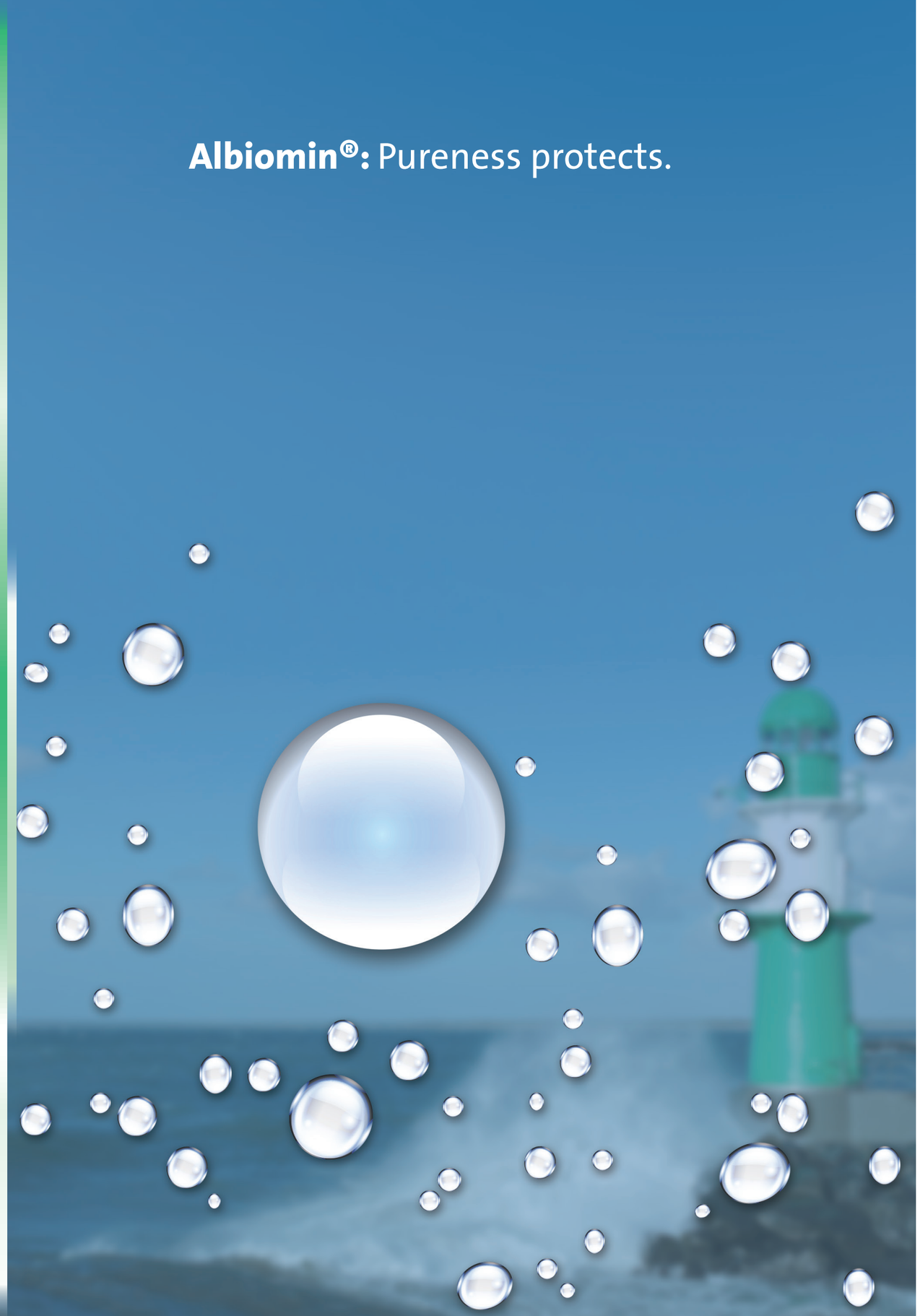


Indications for use:

Acute volume loss

- from major blood loss
- from major burns (but not in the first 24 hours)
- in liver surgery, liver transplantation
- in therapeutic plasmapheresis
- during surgical procedures
- in sepsis
- in ascites

Hypoalbuminemia

- in cirrhosis of the liver and hepatorenal syndrome (HRS)
- in sepsis and multiple organ failure
- in spontaneous bacterial peritonitis (SBP)
- following paracentesis (aspiration of fluid from the abdominal cavity)

Safety:

Quality assurance and viral safety start with plasma sourcing

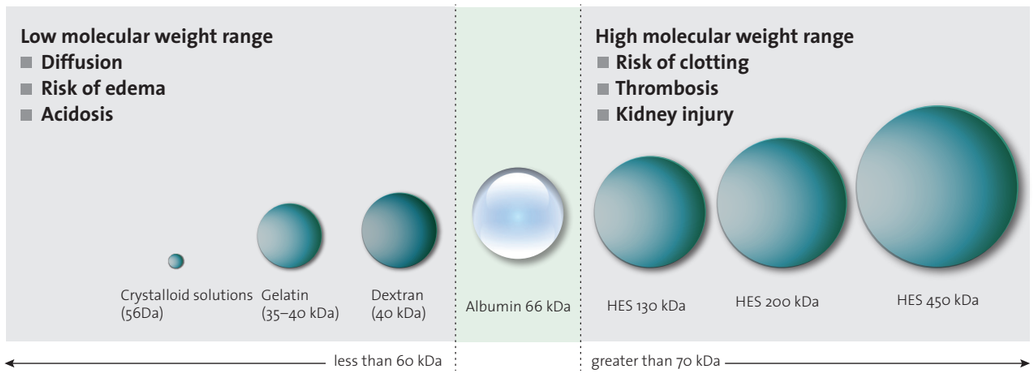
- Only plasma from officially licensed and controlled centers in Germany, Switzerland, Austria, Hungary, the Netherlands, Belgium and the United States is processed for the production of Albiomin®
- Plasma from healthy and "qualified" donors
- A donation will not be used unless and until the donor returns after 60 days for another donation and has been retested for viral markers (all donor plasma is quarantined for 60 days)
- Virologic screening of all donations for HBs antigen and antibodies to HIV-1/-2 and HCV Testing of production plasma pools for HAV, HBV, HCV, HIV and parvovirus B19 by nucleic acid amplification technology

Viral safety and exclusion of procoagulatory activity in the production process

- Protein precipitation steps at various pH values and alcohol concentrations
- Pasteurization at 60 °C for 10 hours

Albiomin®: Molecular size makes the difference

Molecular size of albumin vs. other volume expanders



Human albumin is not only a volume expander of first choice, but a medication

- Maintains colloid osmotic pressure (albumin maintains 80% of COP)
- Acts as a carrier molecule for fatty acids, hormones, enzymes and drugs ✓ Albumin only
- Binds water, calcium, sodium and trace elements ✓ Albumin only
- Has a key role in regulating endothelial permeability (high albumin concentration → reduced permeability) ✓ Albumin only
- Neutralizes toxic products and has antioxidative activity ✓ Albumin only
- Forms a layer on the glycocalyx and neutralizes mediators of inflammation ✓ Albumin only
- Provides a protein reserve for wound healing processes ✓ Albumin only

The side effect profile of synthetic colloids includes:

- Accumulation in tissues (organs and skin): HES[5,12,13,15,]
- Treatment-resistant pruritus: HES[13,15]
- Anaphylactic reactions: HES, gelatin and dextran[3,11,17]
- Rapid metabolic breakdown and short half-life: gelatin[9,23,26]
- Increased clotting/thrombotic risk: HES, dextran and gelatin[3,12,17,20,23,28]
- Increased risk of kidney and liver injuries: HES and dextran[3,4,9,12,14,22,23,25,26,27,31]

Albiomin®: Favorable side effect profile

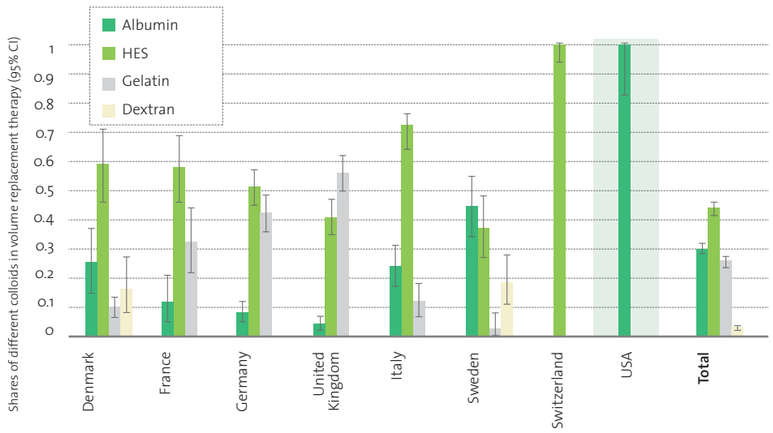
Human albumin has important regulating functions that synthetic colloids cannot provide or only with limitations. In addition, human albumin has a favorable side effect profile compared to synthetic colloids[3].

If colloids, then albumin!

Volume replacement therapy is increasingly relying on a combination of crystalloids and human albumin. In routine clinical practice, colloids are often needed because low-molecular-weight crystalloid solutions (NaCl, RL) diffuse rapidly and maintenance of colloid osmotic pressure – following major blood or fluid loss for example – can primarily be achieved with colloids or a combination of crystalloids and colloids.

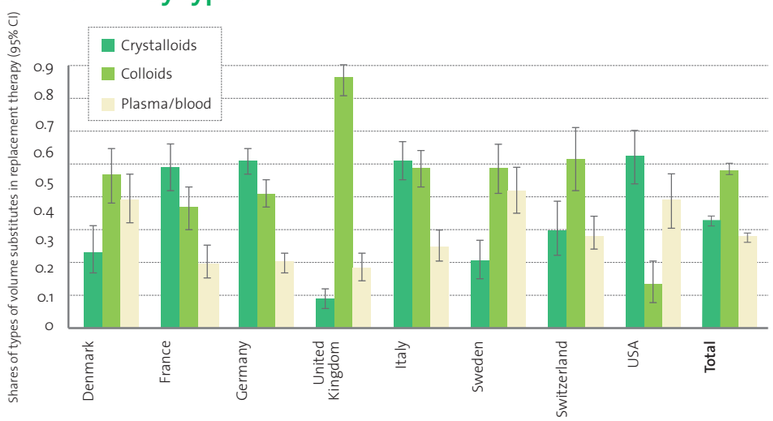
In the United States, for example, volume replacement therapy, apart from using crystalloids, almost exclusively relies on human albumin as a colloid, particularly because of the excellent colloid osmotic effect of albumin and its favorable side effect profile.

Volume replacement therapy – international comparison
Distribution of colloids[10]



The significance of albumin is growing. USA: "If colloids, then albumin!"

Volume replacement therapy – international comparison
Distribution by types[10]



Volume replacement therapy: colloids tend to hold the largest market shares

Albiomin®: low sodium concentration

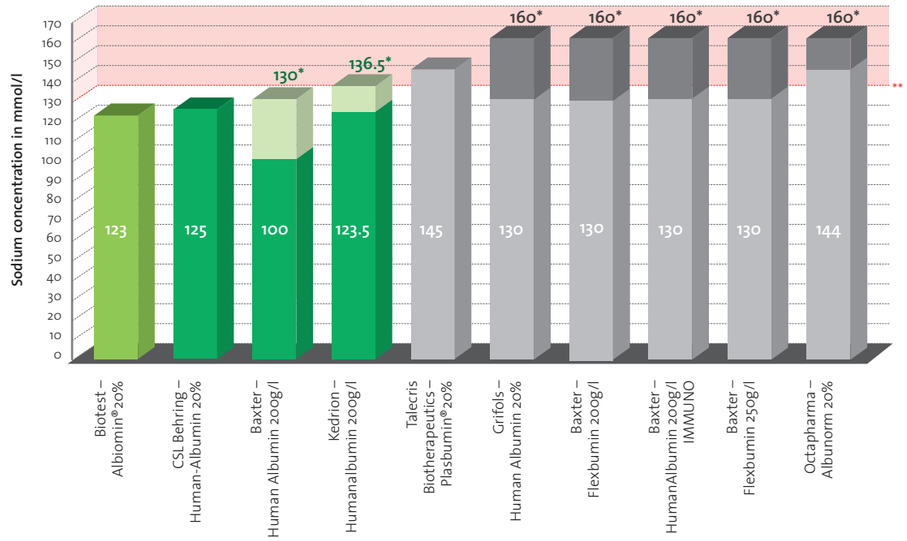
A high sodium concentration may lead to blood pressure increase and acidosis.

- Patients at risk include those with hypertension, renal impairment, diabetes, pronounced edema, congestive heart failure and the elderly.[16]

NaCl (Na+) maximum daily dose:[16]

2300 mg (~900 mg)	General population
1500 mg (~600 mg)	High-risk groups (hypertension, heart failure and renal impairment, diabetes, etc.)

Sodium concentration: Albiomin 20% vs. competitors



* Two-colored: sodium concentration range, all values according to the SmPC/Prescribing Information

** At a dose of 200 mL of 20% human albumin, the maximum daily dose of Na+ for high-risk groups (~600 mg) is attained at approximately 130 mmol.

Albiomin® 20% has a low sodium concentration

Sodium concentration of plasma : **140 mmol/L** (= 3.2 g/L)
Albiomin® 20%: 123 mmol/L sodium ions (= 2.8 g/L)

Albiomin®: low aluminum concentration

Aluminum accumulates in the body:

- when the gastrointestinal tract is bypassed, e.g., during an infusion, or in case of renal impairment.[1,6,7,8,18,19,21,24,29,30]

A high aluminum concentration may lead to aluminum poisoning.[1,2,6,7,8,18,19,21,24,29,30]

► Patients at risk include those with renal impairment or burns, neonates and preterm infants and the elderly

If a significant load exceeds the body's excretory capacity, the excess aluminum is deposited in various body tissues:[1,18,19,24,29]

- Bone
- Brain
- Liver
- Heart
- Spleen
- Muscle

Aluminum accumulation has recently been suggested to be associated with the following conditions:[1,2,6,17,18,19,21,24,29,30]

- Muscle weakness
- Bone diseases (defective mineralization and osteomalacia)
- Anemia
- Impaired iron absorption
- Compromised immune system
- Dementia
- Altered mental status
- Oxidative stress of brain tissue (some experts assume that aluminum has a role in Alzheimer's disease)

Intravenously infused aluminum[8,21]**:**

- Up to 74% of infused aluminum accumulates in tissues
- Neonates or patients with renal impairment show increased accumulation of aluminum in tissues

The European Pharmacopoeia prescribes that the aluminum concentration in albumin products **shall be not more than 200 µg/L for hemodialysis patients and preterm infants.**

Aluminum content of Albiomin® ≤ 60 µg/L

Albiomin®: Pureness protects.

- Safety in plasma pool sourcing
- Safety through viral reduction and inactivation steps in the production process
- Low sodium concentration
- Low aluminum concentration
- High albumin purity (determined by CZE)
- High protein content (>99%)
- Favorable side effect profile

Literatur

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Basic information

Name of the medicinal product: Albiomin® 5 % (50 g/l) / Albiomin® 20 % (200 g/l) **Composition: Human Albumin** Albiomin 5% (50g/l) is a solution containing 50 g/l of total protein and Albiomin 20% (200g/l) is a solution containing 200 g/l of total protein of which at least 95% is human albumin. The product has a hyperoncotic effect. **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. **Contraindications:** Hypersensitivity to albumin preparations or to any of the excipients. **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 g/l is approximately four times that of blood plasma. Therefore, when concentrated albumin is administered, care must be taken to ensure adequate hydration of the patient. Patients should be monitored carefully to guard against circulatory overload and 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, 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 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. **Undesirable effects:** Mild reactions 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 as far as shock may occur. In these cases, the infusion should be stopped and an appropriate treatment should be initiated. **Commercial presentaions:** Solution in vial, 250ml (5%), 50ml (20%) und 100ml (20%). **Date of revision of the text:** April 2013