Information for doctors and other medical professionals

kidneys  liver  pancreas  heart

www.biolasol.com
BIOLASOL®

Solution for organs perfusion and preservation. Medical device.

1. General information
1.1. Characteristics of the product

BIOLASOL® is the Solution for organs perfusion and preservation (kidneys, liver, pancreas, heart) in transplantation.

Pharmacotherapeutic group: solutions and diluents, for perfusion, preservation of organs, organ parts or tissues.

ATC code – V07AB
CPV code – 33.69.23.00-0
Class of the medical device – IIa
Certificate – Product in accordance with 93/42/EWG, Reg. No. TNP/MDD/0120/3991/2014 for the IIa category of sterile devices, approved by TÜV Nord, Poland, 06.05.2015.

Registration by the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products [266/2015].

2. Product description
2.1. Composition

One bag of the volume of 100 ml/1l of BIOLASOL® solution contains:

<table>
<thead>
<tr>
<th>NAME</th>
<th>CONCENTRATION [mmol/l]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextran 70 kDa</td>
<td>0.7</td>
</tr>
<tr>
<td>Glucose</td>
<td>167</td>
</tr>
<tr>
<td>Tri- sodium citrate dihydrate</td>
<td>30</td>
</tr>
<tr>
<td>Di-sodium edetate</td>
<td>5</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>10</td>
</tr>
<tr>
<td>Magnesium fumarate</td>
<td>5</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>5</td>
</tr>
<tr>
<td>Calcium chloride</td>
<td>0.5</td>
</tr>
<tr>
<td>Water for injection</td>
<td>ad 1000ml</td>
</tr>
</tbody>
</table>

2.2. Form

BIOLASOL® is a clear, colourless (or slightly yellow) solution. The solution has an approximate calculated osmolarity of 330 mOsm/kg, a sodium concentration of 105 mmol/l, a potassium concentration of 10 mmol/l, and a pH of 7.4 at room temperature. BIOLASOL® solution is a sterile and non-pyrogenic solution.

2.3. Application

BIOLASOL® solution is intended for the perfusion and preservation of organs [heart, liver, pancreas and kidneys] in hypothermia, from the moment of graft harvest from the donor, through the transport and storage, to the transplantation in the recipients body. Maximum time of organs storage in BIOLASOL® is 24 h. BIOLASOL® solution is non-invasive medical device for single use.

2.4. The effect of the solution

BIOLASOL® solution is intended for the perfusion and preservation of organs. It is extracellular solution with a sodium concentration of 105 mmol/l and potassium concentration of 10 mmol/l supporting maintenance of the structural-functional integrity of the graft. The effect of BIOLASOL®, which is to minimize ischemic-reperfusion injuries, is gained by the presence of components such as: electrolytes, osmotic and oncotic active substances, buffer systems, substances preventing cell acidosis and substances which constitute an energy source, as well as antioxidants.

2.4.1.

The basic component of the BIOLASOL® solution is Dextran 70 kDa, used due to its low viscosity and isotonic and isooncotic properties in reference to plasma. Its pharmacologic effect is similar to that of the human plasma albumin. Colloidal-osmotic effect of Dextran 70 causes fluids flow from the interstitial to the intravascular area. It affects maintenance of the correct fluid volume in aqueous areas, and what is more, it prevents cells edema. It shows no interference with grafts function, even after the prolonged contact. It has effect on hemostasis by slowing down the coagulation process through the effect on platelets and lowering the concentration of factor VIII, V and IX. It does not cause blood cells coagulation, but also dissolve blood cell aggregates, which improves the blood supply of kidney cortex and increases diuretic effect. The application of Dextran 70 kDa improves capillary circulation, decreases/eliminates blood cells aggregation. Thus, it prevents vascular disorders and organs injury.

2.4.2.

The use of glucose anhydrous as a source of energy allows to refill the deficiency of highly energetic phosphate compounds. It is an osmotic active substance, which does not permeate cell membranes freely, and due to that it allows to regulate fluid distribution in fluid compartments. It has a great impact on the effective molality, maintain osmotic gradient between extra- and intracellular fluid, preventing cells edema.

2.4.3.

Tri-sodium citrate is an in vitro anticoagulation factor. By binding calcium ions it eliminates catalytic effect of calcium in coagulation cascade. Tri-sodium citrate is part of the solution intracellular buffer. It has impact on acid-base homeostasis, prevent
intracellular pH in reference ranges. This helps to keep proper activity of enzymes. Tri-sodium citrate as a main source of sodium cations, which determine extracellular composition of BIOLASOL®.

2.4.4.

Di-sodium edetate is a factor which has ability to chelate cations of d-block metal. By chelation of calcium ions it blocks activation of zymogens, which are involved in the coagulation cascade so it demonstrate anticoagulant properties. Moreover, removes catalytic effect on catabolic reactions by decreasing free ions level. Di-sodium edetate binds ions which are releas from the microsomal fraction of cells during preservation. Additionally, minimizes free radical damage cause by reperfusion.

2.4.5.

Potassium chloride regulates water–electrolyte balance. It is a major source of potassium ions, whose concentration is similar to the extracellular fluid. This composition of components allows accurate graft flush and minimize the risks of cells edema. Replacing the chloride ions which has ability to freely penetrate the lipid bilayer with less penetrating anions prevent cell edema.

2.4.6

Magnesium fumarate is a component which protects chemico-physical properties of BIOLASOL® and ensure other components stability. In addition, fumaric acid directly through reducing properties, and indirectly through activation of transcriptional response genes to oxidative stress factors minimizes which may arise during ischemia and reperfusion. As a source of magnesium ions, magnesium fumarate also affects on lipid bilayer integrity and function. Magnesium can create complex compounds with phospholipids in cell membranes.

Due to that, reduces liquidity and permeability of cell membranes.

2.4.7

Sodium bicarbonate is a part of extracellular buffer which provide homoeostasis in organ intended for transplant. It allows to keep proper pH through the action of compensation acidic metabolites formed as a result of increased anaerobic metabolism. Sodium bicarbonate is also a source of Na + and HCO3- for maintaining electrolyte balance of solution.

2.4.8

Finally, calcium chloride as a source of calcium and chloride ions influences electrolyte balance at the level of extracellular fluid. The calcium ions in a low concentration stabilized cell membrane and protect against calcium paradox during reperfusion.

2.5 Storage conditions

BIOLASOL® is stable for 24 months when stored in temperature range of 2 – 8 °C and 12 months in temperature range 12 - 25° C.

3. Application and arrangements of manufacturer

3.1 Indications

Kidney transplant because of: end-stage kidney disease, which may be associated with the following clinical disorders:

- glomerulonephritis, glomerulopathy, inborn kidney disease, sclerosis of the renal pelvis, pyelonephritis, etc.

Liver transplant because of:

- viral hepatitis leads to necrosis, cholestasis, alcoholic liver disease, cirrhosis in general, liver disease of unknown origin, acute liver failure, autoimmune hepatitis, liver cancer, metabolic disorders to leads to cirrhosis, budd–chiari syndrome, choledochal cysts, toxic cirrhosis.

Pancreas transplant- in patients with type I diabetes who observed significant fluctuations in blood glucose - other indications the same as in kidney transplantation.

Heart transplant because of:

- Adults: coronary artery disease, cardiomyopathy, congenital heart defect, end-stage congenital heart defect, tumors of the heart.
- Children: congenital heart defect, dilated cardiomyopathy, myocarditis, hypertrophic cardiomyopathy, restrictive cardiomyopathy, vitium valvularum cordis, tumors of the heart, coronary artery anomalies

3.2 Safety arrangements

BIOLASOL® solution is intended for single use only. Reusing may carry a risk of infection or cross contamination. BIOLASOL® solution should not be used for in situ organ flushing in living donors. It should not be used for systemic administration by direct injection and intravenous infusion. Before implantation into a receiver, organ should be flushed with 0,9% normal saline solution. Biolasol solution is not administered to organ receivers, so associated undesirable effects should not be expected. BIOLASOL® is contraindicated for use in patients with hypersensitivity to any component of Biolasol's solution.
3.3 Intended users

BIOLASOL® is intended for use by specialized personnel and medical staff.

3.4 Bibliography and references:


3.5 Manufacturer

„Biochefa” Pharmaceutical Research and Production Plant Sp. z o.o.
ul. Kasztanowa 3, 41-205 Sosnowiec, Poland
‘Biochefa’ is a respected scientific-research center.

The mission of ‘Biochefa’ is providing customers with high quality products having a guaranteed efficiency of action. A continuous striving for perfection in our production is assured by well-trained staff and numerous investments in modern, well-equipped production facilities and technological, research and microbiological laboratories.

The company is working on the basis of ISO 9001 and ISO 13485 quality standards, certification was granted in 2013 for medicinal products and dietary supplements manufacturing.

The company offers a wide range of mineral-vitamin supplements in form of tablets, tinctures containing natural ingredients, veterinary products and biocides manufactured under most up-to-date technologies and strict quality standards. ‘Biochefa’ is active on the Polish market and also exports products to the whole European Union, Russia, Finland and Canada.

Company’s main targets in terms of scientific research include: advanced studies on isolation, purification and activity of protein hormones, development of perfusion and preservation solutions used in transplantation and dietary supplement technology. Results of above-mentioned studies are in most patented and commercially implemented.