BIOPHARMA. MORE THAN 120 YEARS

of experience in manufacture of blood plasma-derived medicinal products

GMP
ISO 9001:2008
ISO 14001: 2005

biopharma

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INN	ATX	Brand	Presentation form
Albumin	B05AA01	Albumin-Biopharma	10% and 20% solution for infusion in 50 mL or 100 mL vial
Immunoglobulin normal human for intravascular adm.	J06BA02	Bioven	10% solution for infusion in 25 mL, 50 mL or 100 mL vial
Immunoglobulin normal human for intravascular adm.	J06BA02	Bioven Mono	5% solution for infusion in 25 mL, 50 mL or 100 mL vial
Von Willebrand factor and coagulation factor VIII in comb.	B02BD	BioClot A	lyophilisate for solution for injection 250 IU (250 IU of coagulation factor VIII, 125 IU of von Willebrand factor); 500 IU (500 IU of coagulation factor VIII, 250 IU of von Willebrand factor); 1,000 IU (1,000 IU of coagulation factor VIII; 500 IU of von Willebrand factor); in vial No.1 with a solvent (water for injections in a 5 mL or 10 mL vial) and a vehicle for administration
Anti-D (rh0) immunoglobulin	J06BB01	Immunoglobulinum humanum antirhesus Rh0 (D)	solution for injection, 1.0 mL in an ampoule No. 1
Ceruloplasmin	B05AA02	Biocerulin	solution for injection, 100 mL/dose, in ampoules No. 5
N/A	B02BC	Spongia haemostatica	0.8 g in a vial No.1

ALBUMIN-BIOPHARMA

INN: albumin

PF: 10 % and 20 % solution for infusion in 50 mL or 100 mL vial

ATX: B05AA01

THERAPEUTIC INDICATIONS[1]:

recovery and maintenance of BCV (volume of circulating blood) when there is a sign of insufficient volume and the need for the use of colloids[1]

Conditions for which administration of albumin is indicated[2]: shock (haemorrhagic, traumatic, and thermal); acute haemorrhage; purulent-septic conditions; liver disease with a violation of albumin-synthesizing function; hepatic cirrhosis; kidney disease (nephritis, nephrotic syndrome); burn disease; surgeries using artificial circulation; therapeutic plasmapheresis; haemolytic disease of new-borns during the surgery of replacement blood transfusion; preoperative haemodilution; brainoedema; diseases of GIT with impaired suction or patency

ALBUMIN PRODUCTION TECHNOLOGY

WHOLE BLOOD → PLASMAPHERESIS → PLASMA

FREEZING

CRYOPRECIPITATE
SUPERNATANT FLUID
FACTOR [8,9]

REACTOR
(MIXING, THAWING OUT)

PROTEIN FRACTIONS

CENTRIFUGING

Alcohol fractionation
ULTRAFILTRATION
STABILIZATION
PASTEURIZATION

ALBUMIN
GLOBULIN

Albumin 20 % – the gold standard of natural colloidal preparations[2]
Albumin-Biopharma complies with the European Pharmacopoeia regulations on quality, purity and safety parameters[3,4]

1. Instruction for medical use of Albumin-Biopharma (M.A. UA/15875/01/01, UA/15875/01/01 dated 20.03.2017) http://www.drlz.com.ua/
2. Черний В.И. Роль и место альбумина в современной ИТТ: МНС-№1(80).-С.21-25
3. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 01/2013:0255. Human albumin solution. - P. 2404-2406
4. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 01/2014:0853. Human plasma for fractionation. - P. 2425-2426

ABSOLUTE INDICATIONS FOR ALBUMIN ADMINISTRATION:

albumin level below 25 g/l or colloid osmotic pressure below 15 mmHg

Decreased plasma albumin concentration for every 2.5 g/L increased risk of death by 24-56 % (e.g., in post-surgery patients)

- In heart operations, the administration of albumin reduces the need for fluid administration and the severity of pulmonary oedema[1]
- In patients with ascites, albumin administration reduces period of hospitalization, and survival after bacterial peritonitis[1]
- Albumin in high doses reduces the incidence rate in patients with hypoalbuminemia[1]
- When using albumin in patients with burns, complications occur less often than after administration of crystalloid solutions[1]
- The inclusion of albumin in the treatment regimen improves the outcome of the disease in patients with brain damage[1]
- Albumin safety and efficacy profiles surpass those of synthetic colloids during resuscitation in critically ill patients[2-5]
- The use of albumin after paracentesis prevents the development of renal failure and hyponatremia even when removing 10 litres of fluid[6]

1. GR Haynes, RJ Navickis, и MM Wilkes. Albumin administration: what is the evidence of clinical benefit? A systematic review of randomized controlled trials. Eur J Anaesthesiol. 2003 Oct;20(10):771-93
2. Zazzerona L., Gattinonib L., Caironia P. Role of albumin, starches and gelatins versus crystalloids in volume resuscitation of critically ill patients // Curr Opin Crit Care. – 2016
3. Haynes G.R., Navickis R.J., Wilkes M.M. 2003 Albumin administration — what is the evidence of clinical benefit? A systematic review of randomized controlled trials
4. Wilkes M., Navickis R., 2001 Wilkes M.M., Navickis R.J. Patient survival after human albumin administration. A meta-analysis of randomized, controlled trials
5. Von Hoegen I., Waller C. 2001 Safety of human albumin based on spontaneously reported serious adverse events
6. Gines P., Tito L., Arroyo V., et al. Randomized Comparative Study of Therapeutic Paracentesis With and Without Intravenous Albumin in Cirrhosis / P. // Gastroenterology. 1988 Jun;94(6):1493-502

BIOVEN, BIOVEN MONO

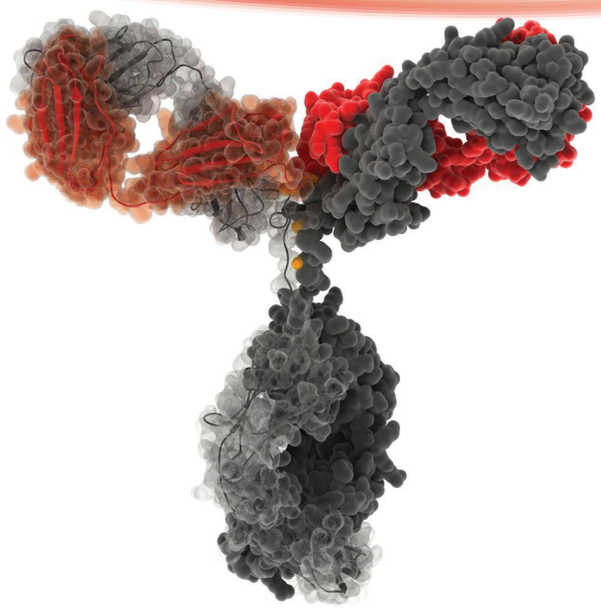
INN: Immunoglobulin, normal human, for intravascular adm.
PF: 5 % or 10 % solution for infusion in 25 mL, 50 mL or 100 mL vial
ATX: J06BA02

THERAPEUTIC INDICATIONS[1]:

cytopoenia of various genesis; thrombocytopenic purpura; severe bacterial, toxic and viral infections; polyneuropathy; primary and secondary immunodeficiencies; autoimmune diseases

- Colt meets the requirements of the European Pharmacopoeia for quality, purity and safety of the finished product and raw materials[2-3]
- The use of the ion-exchange chromatographic purification method makes it possible to qualify these medicinal products as the next 4th generation IG, due to which they have a high safety profile[1]
- It contains more than 99 % of structurally and functionally complete molecules of monomeric IgG[1,4]
- It has two validated stages of virus inactivation, including SD treatment – the world's gold standard[5]
- Donors undergo examination for the absence of antigen and antibodies to HIV 1 and 2, hepatitis C virus; plasma pools are tested by means of ELISA for the absence of HBsAg, antigen and antibodies to HIV 1 and 2, antibodies to hepatitis C virus, and by means of PCR method for the content of nucleic acids of hepatitis C and B viruses; parvovirus B-19 and HIV-1 and HIV-2[1,4]
- It is possible to use in new-borns and pregnant women[1]
- T ½ = 27.24+/-10.74 days

BIOVEN. DISTRIBUTION OF IGG SUBCLASSES



One of the requirements of the European Pharmacopoeia reads:

distribution of IgG subclasses should correspond to the physiological

Subclass	Physiological distribution range, %	Distribution range in Bioven, %
G1	36 – 81.5	57
G2	14 – 47	37
G3	1.5 – 8	3
G4	0.6 – 10.4	3

1. BIOVEN MONO Instruction for medical use of the medicinal product (M.A. UA/14526/01/01 of July 15, 2015); BIOVEN (M.A. UA/14526/01/02 of June 21, 2016) http://www.drlz.com.ua/
2. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 01/2014:0853. Human plasma for fractionation. - P. 2425-2426
3. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 01/2012:0918. Human normal IG for i/v adm. - P. 2423-2425
4. Certificate of analysis for BIOVEN, 10 % solution for infusions 25 mL in vial No.1. Batch No. 10815
5. http://www.biofarma.ua/en/proizvodstvo-biofarma/tekhnologii.html

BIOCLOT A

INN: Von Willebrand factor and coagulation factor VIII in combination

PF: lyophilisate for solution for injection
250 IU (250 IU of coagulation factor VIII, 125 IU of von Willebrand factor);
500 IU (500 IU of coagulation factor VIII, 250 IU of von Willebrand factor);
1,000 IU (1,000 IU of coagulation factor VIII; 500 IU of von Willebrand factor);
in vial No. 1 with a solvent (water for injections in a 5 mL or 10 mL vial) and a vehicle for administration

ATX: B02BD06

THERAPEUTIC INDICATIONS[1]:

treatment and prevention of bleeding caused by congenital or acquired Factor VIII deficiency (haemophilia A); von Willebrand disease with coagulation factor VIII deficiency

- It meets the requirements of the European Pharmacopoeia for quality, purity and safety of the finished product and raw materials[2-4]
- It has two validated stages of virus inactivation, including SD treatment – the world's gold standard[5]
- Factor VIII activity rate in blood plasma upon administration of 80–120 % of the expected one[1]
- It undergoes regular testing at the Paul-Ehrlich-Institut, Federal Institute for Vaccines and Biomedicines (Langen, Germany)[6]
- The pharmacokinetic profile corresponds to standard profile for blood coagulation plasma factor drugs[7]

1. BIOCLOT Instruction for medical use of the medicinal product (M.A. 883/12-300200000 dated 03.06.2016) http://www.drlz.com.ua/
2. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 01/2014:0853. Human plasma for fractionation. - P. 2425-2426
3. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 07/2013:0275. Human coagulation factor VIII. - P. 2414-2415
4. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 07/2013:2298. Human von Willebrand factor. - P. 2435-2436
5. http://www.biofarma.ua/en/proizvodstvo-biofarma/tekhnologii.html
6. http://www.pei.de
7. Ющенко П.В. соавт. ОВРЕМЕННЫЕ ПРИНЦИПЫ ЛЕЧЕНИЯ ПАЦИЕНТОВ С ГЕМОФИЛИЕЙ А, ОСЛОЖНЕННОЙ ГЕМАРТРОЗАМИ КРУПНЫХ СУСТАВОВ. ГЕМАТОЛОГИЯ. ТРАНСФУЗИОЛОГИЯ. ВОСТОЧНАЯ ЕВРОПА, 2016: No.4. - С. 507-520
8. Giangrande PLF et al. Kreuth IV: European consensus proposals for treatment of haemophilia with coagulation factor concentrates. Haemophilia. 2017 May;23(3):370-375. doi: 10.1111/hae.13211. Epub 2017 Apr 12

In accordance with the recommendations of Kreuth IV Meeting, the minimum level of consumption of factor VIII concentrate in any country should be 4 IU per capita of general population[8]

FACTOR VIII WITHOUT VON WILLEBRAND FACTOR (2018), FACTORS VII, IX, AND XI (2019–2020) ARE UNDER DEVELOPMENT

IMMUNOGLOBULINUM HUMANUM ANTIRHESUS RH0 (D)

INN: anti-D (rh0) immunoglobulin
PF: solution for injection, 1.0 mL in an ampoule No. 1
ATX: J06B B01

THERAPEUTIC INDICATIONS[1]:

for prevention in the pre- and postnatal period in Rh-negative women that are unresponsive to Rh0 (D) antigen; with artificial termination of pregnancy in Rh-negative women, unresponsive to Rh0 antigen in case of Rh-positive blood belonging to a husband; with miscarriage or threat of miscarriage; when performing amniocentesis; with injuries of the abdominal cavity during pregnancy

- It meets the requirements of the European Pharmacopoeia for quality, purity and safety of the finished product and raw materials[2,3]
- It has two validated stages of virus inactivation, including SD treatment – the world's gold standard[4]
- Donors undergo examination for the absence of antigen and antibodies to HIV 1 and 2, hepatitis C virus; plasma pools are tested by means of ELISA for the absence of HBsAg, antigen and antibodies to HIV 1 and 2, antibodies to hepatitis C virus, and by means of PCR method for the content of nucleic acids of hepatitis C and B viruses; parvovirus B-19 and HIV-1 and HIV-2[1,4]
- Ready-to-use[1]

In general, the policy of prescribing anti-D immunoglobulin at week 28 and 34 during pregnancy for all women with negative Rh (D) leads to a decreased alloimmunization from ~ 1 % to ~ 0.3 % (NICE)[5]
Decreased sensitization leads to a reduction in mortality from 46/100.000 births to 1-6/100.000 births (Pilgrim et al., 2009)

1. IMMUNOGLOBULINUM HUMANUM ANTIRHESUS Rh0(D) Instruction for medical use of the medicinal product (M.A. UA/13033/01/01 of August 21, 2017) http://www.drlz.com.ua/
2. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 01/2014:0853. Human plasma for fractionation. - P. 2425-2426
3. European Pharmacopoeia Commission, Council of Europe European Directorate for the Quality of Medicines (EDQM). European Pharmacopoeia. 8th edition, 2013. 07/2008:0557. Human anti-D IG. - P. 2406
4. http://www.biofarma.ua/en/proizvodstvo-biofarma/tekhnologii.html
5. National Institute for Clinical Excellence (NICE). Guidance on the use of routine antenatal Anti-D prophylaxis for Rh (D) negative women. 2008. Available from: http://www.nice.org.uk/guidance/index.jsp?action=byID&o=12047

BIOCERULIN

INN: ceruloplasmin

PF: solution for injection, 100 mL/dose in ampoules No. 5

ATX: B05AA02

THERAPEUTIC INDICATIONS[1]:

to reduce intoxication during complex combined chemotherapy in oncological patients, including patients with haemoblastosis and moderate intoxication; preoperative preparation, especially of debilitated patients – with anaemia, intoxication and exhaustion;
In the early postoperative period (with massive blood loss, purulent-septic complications);
to stimulate haemopoiesis; in a combined therapy of patients with osteomyelitis

- Ceruloplasmin is an essential extracellular blood antioxidant[2]
- By 60-fold more potent than other antioxidants[2]
- It inhibits lipid peroxidation (LPO) by 50 %[2]
- It is the company's unique development[3]
- It has pronounced detoxification properties[1]

1. BIOCERULIN Instruction for medical use of the medicinal product (M.A. UA/0763/01/01 dated 27.04.2017) http://www.drlz.com.ua/
2. Коровина Н А, Захарова И Н , Обыночная Е Г Применение антиоксидантов в педиатрической практике
3. https://www.health-ua.org/faq/gepatologiya/2465.html

SPONGIA HAEMOSTATICA

INN: n/a

PF: dry substance 0.8 g in a vial No.1

ATX: B02B C

THERAPEUTIC INDICATIONS[1]:

local capillary and parenchymal haemorrhages, bleeding from bones, muscles or tissues; bleeding localized on the surface of the body or in its cavities; nasal, gum bleeding or bleeding in patients with thrombocytopenic purpura, leukaemia, haemorrhagic thrombocytopathy, Osler-Randu syndrome, hepatic cirrhosis, and chronic nephritis

- Topical action: does not increase the prothrombin index and has no adverse effect on the haemostasis system[1]

1. Spongia haemostatica Instruction for medical use of the medicinal product (M.A. UA/5711/01/01 dated 06.04.2017) http://www.drlz.com.ua/

BIOPHARMA: QUALITY CONTROL SYSTEM FOR BLOOD PRODUCTS

Careful selection of donors and plasma

1. Import of plasma from EU countries or collection of plasma in Ukraine
2. Each donor undergoes mandatory medical examination
3. Donor blood is tested for viruses
4. a 6-month quarantine of plasma, after which a repeated examination of donors should be carried out

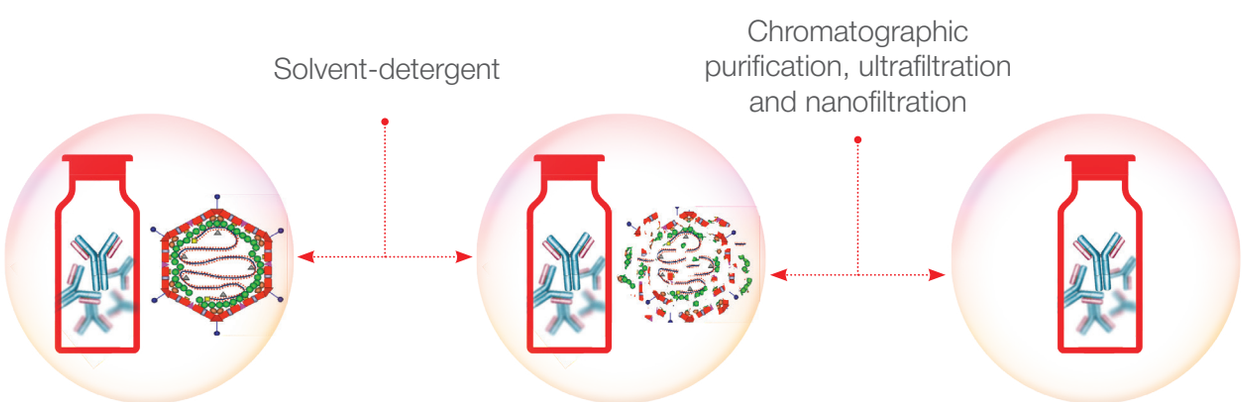
Quality control of plasma

1. Plasma samples are tested by ELISA, PCR
2. After pooling the plasma, re-testing for virus safety is performed

International standards of viral decontamination of plasma

1. Alcohol fractionation of plasma
2. Processing of semi-finished products at low pH
3. Heat treatment
4. Solvent/detergent inactivation of viruses followed by chromatographic purification
5. Ultrafiltration

Treatment with solvent/detergent reliably destructs the lipid envelope of viruses (hepatitis B and C virus, HIV-1 and HIV-2)



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