

MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

PHARMACOPOEIA MONOGRAPH

Human albumin

PM.3.3.2.0006.15

ograph 42-122-04

Replaces the Pharmacopoeia Mon-

The present Pharmacopoeia Monograph applies to human albumin preparations and 5 % , 10 % , 20 % , and 25 % solutions for infusion containing the main human donor plasma protein.

MANUFACTURE

Albumin preparations are manufactured from healthy donors' plasma that should meet the requirements established by the Pharmacopoeia Monograph "Human plasma for fractionation".

Human albumin preparations and solutions for infusion are obtained with the modified alcohol method for fractionation of serum proteins at low temperatures. The manufacture of albumin should guarantee preservation of the structure and function of the protein albumin, ensure the specific and viral safety of the medicinal product, and preclude contamination with foreign agents.

The human albumin solution is heated at 60 °C for not less than 10 hours, and then kept at (30 – 32) °C for 14 days or at (20 - 25) °C for not less than 4 weeks. After that, the solution is evaluated by visual examination for signs of microbial contamination.

Albumin contains stabilizers: sodium caprylate, N-acetyl-tryptophan, or a combination of these.

No antimicrobial preservatives are used in the manufacturing process.

TESTS

Description. A transparent or slightly opalescent, yellow, amber, or greenish

solution. The test is carried out by visual examination.

Identification

Species specificity. The medicinal product should contain only human serum proteins. The test is carried out by gel immunoelectrophoresis, using sera against human, bovine, horse, and porcine serum proteins, as described in the General Pharmacopoeia Monograph “Agarose gel immunoelectrophoresis”. The test may also be performed by gel immunodiffusion, in accordance with the General Pharmacopoeia Monograph “Gel immunodiffusion”.

Principal protein component. The medicinal product should contain a principal protein component that should have the mobility of human albumin. The test is carried out by cellulose acetate electrophoresis, in accordance with the General Pharmacopoeia Monograph “Homogeneity testing for medicinal products containing human or animal serum by cellulose acetate electrophoresis”.

Blood pigments. The optical density of the tested 1 % aqueous albumin solution at wavelength 403 nm in a cuvette with an optical path length of 10 mm should be not more than 0.15 versus water. The test is carried out in accordance with the General Pharmacopoeia Monograph “Spectrophotometry”.

Extractable volume. The extractable volume should be not less than the nominal value. The test is carried out in accordance with the General Pharmacopoeia Monograph “Extractable volume for parenteral pharmaceutical forms”.

Heat stability. The medicinal product should remain unchanged after 50-hour heating at (56 ± 1) °C. The test is carried out by visual examination.

pH value. From 6.5 to 7.2. The test is carried out by potentiometry, in accordance with the General Pharmacopoeia Monograph “Ionometry”.

Fractional composition. The content of albumin should be not less than 97 %, and the content of α - and β -globulins not more than 3 %. The test is carried out by cellulose acetate electrophoresis, in accordance with the General Pharmacopoeia Monograph “Homogeneity testing for medicinal products containing human or animal serum by cellulose acetate electrophoresis”.

Protein content.

From 4.5 % to 5.5 % for 5 % albumin solution.

From 9.0 % to 11.0 % for 10 % albumin solution.

From 18.0 % to 22.0 % for 20 % albumin solution.

From 22.5 % to 27.5 % for 25 % albumin solution.

The test is carried out by an appropriate test method, in accordance with the General Pharmacopoeia Monograph “Determination of protein”.

Polymers and aggregates. The content of polymers and aggregates should not exceed 5.0 %. The test is carried out by size-exclusion high-performance liquid chromatography, in accordance with the General Pharmacopoeia Monograph “High-performance liquid chromatography”.

Sodium caprylate. Not more than 0.23 mmol/g. The test is carried out by size-exclusion high-performance liquid chromatography, in accordance with the General Pharmacopoeia Monograph “High-performance liquid chromatography”.

Prekallikrein activator. Not more than 35 IU/mL. The test is carried out by the chromogenic method.

Aluminium. Not more than 200 µg/L. The test is carried out by atomic absorption spectrometry, in accordance with the General Pharmacopoeia Monograph “Atomic emission spectrometry”.

Sodium ion. From 90 mmol/L to 160 mmol/L. The test is carried out by flame photometry, in accordance with the General Pharmacopoeia Monograph “Atomic emission spectrometry”.

Potassium ion. Not more than 0.05 mmol/L. The test is carried out by flame photometry, in accordance with the General Pharmacopoeia Monograph “Atomic emission and atomic absorption spectrometry”.

Pyrogenicity or Bacterial endotoxins. The medicinal product is required to be non-pyrogenic or its content of bacterial endotoxins should not exceed 0.5 EU/mL for 5 % albumin solution, 1.3 EU for 10 % and 20 % albumin solutions, and 1.7 EU for 25 % albumin solution. The test is carried out in accordance with the General Pharmacopoeia Monograph “Pyrogenicity”. The test dose is 10 mL of the medicinal product per kilogramme of rabbit body weight for 5 % albumin solu-

tion and 5 mL of the medicinal product per kilogramme of rabbit body weight for 10 %, 20 %, and 25 % albumin solutions, or as required by the General Pharmacopoeia Monograph “Bacterial endotoxins”.

Sterility. The medicinal product is required to be sterile. The test is carried out in accordance with the General Pharmacopoeia Monograph “Sterility”.

Viral safety

Hepatitis B virus surface antigen (HBsAg). The medicinal product should contain no hepatitis B virus surface antigen. The test is carried out by enzyme immunoassay, using test systems approved for use in Russian health care practice and having a sensitivity not less than 0.1 IU/mL according to the Instructions for Use.

Anti-hepatitis C virus antibodies. The medicinal product should contain no anti-hepatitis C virus antibodies. The test is carried out by enzyme immunoassay, using test systems approved for use in Russian health care practice and having 100 % sensitivity and specificity according to the Instructions for Use.

Anti-human immunodeficiency virus (HIV-1 and HIV-2) antibodies and HIV-1 p24 antigen. The medicinal product should contain no anti-human immunodeficiency virus (HIV-1 and HIV-2) antibodies and no HIV-1 p24 antigen. The test is carried out by enzyme immunoassay, using test systems approved for use in Russian health care practice and having 100 % sensitivity and specificity according to the Instructions for Use.

Packaging and Labeling. In accordance with the General Pharmacopoeia Monograph “Medicinal products containing human plasma”.

Storage. In the temperature range of 2 to 10 °C, away from light.