

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Megalotect 50 U/ml Solution for Infusion, glass infusion bottle.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human normal immunoglobulin (IVIg) with antibodies to cytomegalovirus.

1 ml contains:

Active substance:

| | | |
|---|--------|----|
| Human plasma protein | 100.0 | mg |
| thereof immunoglobulin G (IgG) | ≥ 95.0 | % |
| with antibodies to cytomegalovirus | ≥ 50.0 | U* |
| *Units of the Paul-Ehrlich-Institut reference preparation | | |

Distribution of IgG subclasses:

| | | |
|------|----------|---|
| IgG1 | ca. 62.0 | % |
| IgG2 | ca. 34.0 | % |
| IgG3 | ca. 0.5 | % |
| IgG4 | ca. 3.5 | % |

| | | |
|--------------------------------|---------|-------|
| Immunoglobulin A (IgA) content | max.5.0 | mg/ml |
|--------------------------------|---------|-------|

Excipients

| | | |
|-----------------|-------|----------|
| Sodium chloride | 155.0 | micromol |
|-----------------|-------|----------|

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Infusion.

The solution is clear to slightly opalescent and colourless to pale yellow.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prophylaxis of clinical manifestations of cytomegalovirus infection in patients subjected to immunosuppressive therapy, particularly in transplant recipients.

4.2 Posology and method of administration

Posology:

As a rule doses containing 50 units of (PEI) per kg body weight should be administered. Administration should be initiated on the day of transplantation or the day prior to this (bone marrow transplantation).

An initiation of prophylaxis up to 10 days before transplantation can also be envisaged, particularly in CMV sero-positive patients. A total of at least 6 doses at 2 to 3 weeks' intervals should be given.

Method of administration:

Megalotect should be infused intravenously at a rate of max. 20 drops (1 ml) per minute.

4.3 Contraindications

Megalotect is contra-indicated in patients who are intolerant to homologous immuno-globulins, as for example in those rare cases of IgA or IgG deficiencies.

4.4 Special warnings and precautions for use

Megalotect contains 0.155mmol (3.565mg) sodium per ml. To be taken into consideration by patients on a controlled sodium diet.

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.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV. The measure taken may be of limited value against non-enveloped viruses such as HAV and parvovirus B19.

There is reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to viral safety.

It is strongly recommended that every time that Megalotect 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 Interaction with other medicinal products and other forms of interaction

Live attenuated virus vaccines

Immunoglobulin administration may impair for the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella for a period of at least 6 weeks and up to 3 months. After administration of this product, an interval of 3 months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to 1 year. Therefore patients receiving measles vaccine should have their antibody status checked.

Interference with serological testing

After injection of immunoglobulin the transitory rise of the various passively transferred antibodies in the patients blood may result in misleading positive results in serological testing.

Passive transmission of antibodies to erythrocyte antigens, e.g. A, B D may interfere with some serological tests for red cell allo-antibodies (e.g. Coombs test).

4.6 Fertility, pregnancy and lactation

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given with caution to pregnant women and breast-feeding mothers. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, on the foetus and the neonate are to be expected.

Immunoglobulins are excreted into the milk and may contribute to the transfer of protective antibodies to the neonate.

4.7 Effects on ability to drive and use machines

There are no indications that Megalotect may impair the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions such as chills, headache, fever, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate low back pain may occur occasionally.

Rarely, immunoglobulins may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no sensitivity to previous administration.

Cases of reversible aseptic meningitis, isolated cases of reversible haemolytic anaemia/haemolysis and rare cases of transient cutaneous reactions, have been observed with human normal immunoglobulin.

Increase in serum creatinine level and/or acute renal failure have been observed.

Thrombotic events have been reported in the elderly, in patients with signs of cerebral or cardiac ischemia, and in overweight and severely hypovolaemic patients.

For information on viral safety see section 4.4, Special warnings and precautions for use.

4.9 Overdose

Overdose may lead to fluid overload and hyperviscosity, particularly in patients at risk, including elderly patients or patients with renal impairment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Human immunoglobulin for intravenous administration with antibodies to cytomegalovirus.

ATC code: J 06 BB 09

Megalotect is an immunoglobulin preparation from the plasma of donors who possess a high antibody titre against cytomegalovirus.

5.2 Pharmacokinetic properties

Megalotect is immediately and completely bioavailable in the recipients circulation after intravenous administration. It is distributed relatively rapidly between plasma and extravascular fluid; after approximately 3-5 days an equilibrium is reached between the intra- and extra-vascular compartments. Megalotect has a half-life of about 3 weeks. This half-life may vary from patient to patient, in particular in primary immunodeficiency.

IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body.

In animals, single dose toxicity testing is of no relevance since higher doses result in overloading. Repeated dose toxicity testing and embryo-foetal toxicity studies are impracticable due to the induction of, and interference with antibodies. Effects of the product on the immune system of the newborn have not been studied.

Since clinical experience provides no hint for tumorigenic or mutagenic effects of immunoglobulins, experimental studies, particularly in heterologous species, are not considered necessary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6, Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product.

6.3 Shelf life

3 years.
The solution should be administered immediately after opening the receptacle. Any unused solution must be discarded because of bacterial contamination risk.

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C).
Do not freeze.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

50 ml solution in a Type II glass infusion bottle.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Megalotect should be warmed to room or body temperature before administration.
Parenteral products should be inspected visually for particulate matter and discoloration prior to administration.
The solution should be clear or slightly opalescent.
Do not use solutions which are cloudy or which have deposits.
Any unused product or waste material should be disposed of in accordance with local requirements.
Megalotect is miscible with physiological saline solution.

7 MARKETING AUTHORISATION HOLDER

Biotest Pharma GmbH
Landsteinerstraße 5
D-63303 Dreieich
Germany

8 MARKETING AUTHORISATION NUMBER

PA0592/004/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 April 1995

Date of last renewal: 21 April 2010

10 DATE OF REVISION OF THE TEXT

October 2012