

Package leaflet: Information for the user

KIOVIG 100 mg/ml solution for infusion Human normal immunoglobulin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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2. What you need to know before you use KIOVIG
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1. What KIOVIG is and what it is used for

KIOVIG belongs to a class of medications called immunoglobulins. These medicines contain human antibodies, which are also present in your blood. Antibodies help your body to fight infections. Medicines like KIOVIG are used in patients who do not have enough antibodies in their blood and tend to get frequent infections. They can also be used in patients who need additional antibodies for the cure of certain inflammatory disorders (autoimmune diseases).

KIOVIG is used for

Treatment of patients who do not have sufficient antibodies (replacement therapy). There are two groups:

1. Patients with inborn lack of antibody production (primary immunodeficiency syndromes).
2. Secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either **proven specific antibody failure (PSAF)*** or serum IgG level of <4 g/l.

*PSAF = failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines

Treatment of patients with certain inflammatory disorders (immunomodulation). There are five groups:

1. Patients who do not have enough blood platelets (primary immune thrombocytopenia, ITP), and who are at high risk of bleeding or will have surgery in the near future.
2. Patients with a disease that is associated with multiple inflammations of the nerves in the whole body (Guillain Barré syndrome).
3. Patients with a disease which results in multiple inflammations of several organs of the body (Kawasaki disease).
4. Patients who suffer from a rare condition characterized by slow progressive asymmetrical weakness of limbs without sensory loss (multifocal motor neuropathy, MMN).

5. Patients who suffer from chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

2. What you need to know before you use KIOVIG

Do not use KIOVIG:

if you are allergic to immunoglobulins or to any other ingredients of this medicine (listed in section 6).

For example, if you have an immunoglobulin A deficiency, you may have antibodies against immunoglobulin A in your blood. Since KIOVIG contains trace amounts of immunoglobulin A (less than 0.14 mg/ml), you might get an allergic reaction.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using KIOVIG.

How long monitoring is required during the infusion

- You will be carefully observed during the infusion period with KIOVIG to make sure that you do not suffer a reaction. Your doctor will make sure that the rate at which KIOVIG is infused is suitable for you.
- If KIOVIG is administered at a high rate, if you suffer from a condition with low antibody levels in your blood (hypo- or agammaglobulinemia), if you have not received this medicine before or if there has been a long interval (e.g. several weeks) since you last received it, there may be a higher risk of side effects. In such cases, you will be closely monitored during your infusion and for an hour after your infusion has stopped.
- If you have already received KIOVIG previously and received the last treatment recently, then you will only be observed during the infusion and for at least 20 minutes after your infusion.

When slowing or stopping the infusion may be required

In rare cases your body may have previously reacted to specific antibodies and therefore will be sensitive to medicines containing antibodies. This may happen particularly if you suffer from immunoglobulin A deficiency. In these rare cases, you may get allergic reactions such as a sudden fall in blood pressure or shock even if you have already received treatment with medicines containing antibodies in the past.

If you experience a reaction during the infusion of KIOVIG, tell your doctor immediately. Depending on your doctor's decision the rate of infusion can be slowed or the infusion can be stopped altogether.

Special patient groups

- Your doctor will take special care if you are overweight, elderly, diabetic, or if you suffer from high blood pressure, low blood volume (hypovolaemia), or problems with your blood vessels (vascular diseases). In these conditions, immunoglobulins may increase the risk of cardiac infarction, stroke, lung embolism, or deep vein thrombosis, although only in very rare cases. Tell your doctor if you are diabetic. Although KIOVIG does not contain sugar, it may be diluted with a special sugar solution (5% glucose), which could affect your blood sugar level.
- Your doctor will also take special care if you have or had previously problems with your kidneys, or if you receive medicinal products that may harm your kidney (nephrotoxic medicinal products), as there is a very rare chance of acute kidney failure. Please tell your doctor if you have a kidney disorder. Your doctor will choose the appropriate intravenous immunoglobulin for you.

Information on the source material of KIOVIG

KIOVIG is made from human plasma (the liquid part of blood). When medicines are made from human blood or plasma, a number of measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken for the manufacture of KIOVIG are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus and parvovirus B19. KIOVIG also contains certain antibodies that can prevent an infection with hepatitis A virus and parvovirus B19.

Other medicines and KIOVIG

Tell your doctor or pharmacist if you are taking, or have recently taken or might take any other medicines.

If you have received a vaccination during the last six weeks and up to three months, the infusion of immunoglobulins like KIOVIG may impair the effect of some live virus vaccines such as measles, rubella, mumps and chicken pox. Therefore, after receiving immunoglobulins you may have to wait up to 3 months before receiving your live-attenuated vaccine. You may have to wait for up to 1 year after receiving immunoglobulins before you receive your measles vaccine.

Effects on blood tests

KIOVIG contains a wide variety of different antibodies, some of which can affect blood tests. If you have a blood test after receiving KIOVIG, please inform the person taking your blood or your doctor that you have received the medication.

Pregnancy, breast-feeding and fertility

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
- No clinical trials have been made with KIOVIG in pregnant or breast-feeding women. However, medicines that contain antibodies have been used in pregnant or breast-feeding women, and it has been shown that there are no harmful effects on the course of pregnancy or the baby to be expected.
- If you are breast-feeding and receive KIOVIG, the antibodies of the medicine can also be found in the breast milk. Therefore, your baby may be protected from certain infections.

Driving and using machines

Patients may experience reactions (for example dizziness or nausea) during the treatment with KIOVIG, which might affect the ability to drive and use machines. If this happens, you should wait until the reactions have disappeared.

3. How to use KIOVIG

KIOVIG is intended for intravenous administration (infusion into a vein). It is given to you by your doctor or nurse. Dose and frequency of the infusion will vary depending on your condition and your body weight.

At the beginning of your infusion you will receive KIOVIG at a slow rate. Dependent on how comfortable you are, your doctor may then gradually increase the infusion rate.

Use in children and adolescents

The same indications, dose and frequency of infusion as for adults apply for children and adolescents (age 0 to 18).

If you use more KIOVIG than you should

If you get more KIOVIG than you should, your blood may become too thick (hyperviscous). This could particularly happen when you are a patient at risk, e.g. an elderly patient or a patient having problems with your kidneys. Be sure that you take adequate fluids so you are not dehydrated and notify your physician if you are known to have medical problems.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Certain side effects, e.g. headache or flushing, may be reduced by slowing the infusion rate.

Below is a list of side effects reported with KIOVIG:

- Very common side effects (may affect more than 1 in 10 people):
Headache, high blood pressure, nausea, rash, local reactions (e.g. pain and swelling or other reactions at the infusion site), fever, tiredness.
- Common side effects (may affect up to 1 in 10 people):
Bronchitis, common cold, low red blood cell count, swollen lymph glands, decreased appetite, difficulty in sleeping, anxiety, dizziness, migraine, numbness or tingling of the skin or of a limb, reduced sense of touch, eye inflammation, rapid heartbeat, flushing, cough, runny nose, chronic cough or wheezing (asthma), stuffy nose, sore throat, shortness of breath, diarrhoea, vomiting, abdominal pain, indigestion, contusion, itching and hives, dermatitis, reddened skin, pain in your back, pain in your joints, pain in your arms or legs, muscle pain, muscle cramps, muscular weakness, chills, accumulation of fluid under the skin, influenza-like illness, pain or discomfort in the chest, lack of strength or feeling of weakness, indisposition, shaking chills.
- Uncommon side effects (may affect up to 1 in 100 people):
Chronic infection of the nose, fungal infections, various infections (of the nose and throat, kidney or bladder), sterile inflammation of the layers lining the brain, serious allergic reactions, disorder of the thyroid, excessive response to stimuli, memory impairment, difficulty in speaking, unusual taste in the mouth, impaired balance, involuntary trembling, eye pain or swelling, vertigo, fluid in middle ear, peripheral coldness, vein inflammation, ear and throat swelling, abdominal distension, rapid swelling of the skin, acute inflammation of the skin, cold sweat, increased reaction of the skin to sunlight, excessive sweating also during sleep, muscle twitching, excess of serum protein in the urine, chest tightness, feeling hot, burning sensation, swelling, increased rate of breathing, changes to blood test results.
- Frequency not known (cannot be estimated from available data):
Destruction of red blood cells, life-threatening allergic shock, transient stroke, stroke, low blood pressure, heart attack, blood clot in a major vein, blood clot in the main artery of the lung, accumulation of fluid in the lung, positive result of Coombs test, decreased oxygen saturation in blood, transfusion-related acute lung injury.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system (see below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

Ireland

HPRA Pharmacovigilance

Website: www.hpra.ie

Malta

ADR Reporting

Website:

www.medicinesauthority.gov.mt/adrportal

5. How to store KIOVIG

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is printed on the label and carton after EXP. The expiry date refers to the last day of that month.
- Do not use this medicine if you notice particulate matter or discolouration.
- Do not store above 25°C.
- Do not freeze.
- Keep the container in the outer carton in order to protect from light.

6. Contents of the pack and other information

What KIOVIG contains

- The active substance of KIOVIG is human normal immunoglobulin.
- 1 ml of KIOVIG contains 100 mg of human protein of which at least 98% is immunoglobulin G (IgG).
- The other ingredients (excipients) are glycine and water for injections.

What KIOVIG looks like and contents of the pack

KIOVIG is a solution for infusion in vials of 10, 25, 50, 100, 200 or 300 ml. The solution is clear or slightly opalescent and colourless or pale-yellow.

Not all presentations may be marketed.

Marketing Authorisation Holder

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This leaflet was last revised in 07/2019

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu/>

The following information is intended for healthcare professionals only:

Method of administration

- KIOVIG must only be administered intravenously. Other routes of administration have not been evaluated.
- KIOVIG should be infused intravenously at an initial rate of 0.5 ml/kg bodyweight/hour for 30 minutes. If well tolerated, the rate of administration may gradually be increased to a maximum of 6 ml/kg bodyweight/hour. Clinical data obtained from a limited number of patients also indicate that adult PID patients may tolerate an infusion rate of up to 8 ml/kg BW/hr.
- If dilution to lower concentrations is required prior to infusion, KIOVIG may be diluted with 5% glucose solution to a final concentration of 50 mg/ml (5% immunoglobulin).
- Any infusion-related adverse events should be treated by lowering infusion rates or by stopping the infusion.

Special precautions

- Any infusion-related adverse events should be treated by lowering the infusion rate or by stopping the infusion.
- It is recommended that every time KIOVIG is administered, the name and batch number of the product is recorded.

Incompatibilities

This medicinal product must not be mixed with other medicinal products.

Special precautions for storage

- After dilution to lower concentrations, immediate use is recommended. The in-use stability of KIOVIG after dilution with a 5% glucose solution to a final concentration of 50 mg/ml (5% immunoglobulin) has been demonstrated for 21 days at 2°C to 8°C as well as at 28°C to 30°C; however, these studies did not include the microbial contamination and safety aspects.

Instructions for handling and disposal

- The product must be brought to room or body temperature before use.
- KIOVIG should be inspected visually for particulate matter and discoloration prior to administration. Only clear to slightly opalescent and colourless to pale yellow solutions are to be administered. Do not use if particulate matter or discoloration is observed.
- If dilution is required, 5% glucose solution is recommended. For obtaining an immunoglobulin solution of 50 mg/ml (5%), KIOVIG 100 mg/ml (10%) should be diluted with an equal volume

of the glucose solution. It is recommended that during dilution the risk of microbial contamination is minimised.

- Any unused product or waste material should be disposed of in accordance with local requirements.

Dose recommendations

Indication	Dose	Frequency of injections
Replacement therapy in primary immunodeficiency	starting dose: 0.4-0.8 g/kg maintenance dose: 0.2-0.8 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Replacement therapy in secondary immunodeficiency	0.2-0.4 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Congenital AIDS	0.2-0.4 g/kg	every 3-4 weeks
Hypogammaglobulinaemia (<4 g/l) in patients after allogeneic haematopoietic stem cell transplantation	0.2-0.4 g/kg	every 3-4 weeks to obtain IgG trough level above 5g/l
<u>Immunomodulation:</u>		
Primary immune thrombocytopenia	0.8-1 g/kg or 0.4 g/kg/d	on day 1, possibly repeated once within 3 days for 2-5 days
Guillain Barré syndrome	0.4 g/kg/d	for 5 days
Kawasaki disease	2 g/kg	in one dose in association with acetylsalicylic acid
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	Starting dose 2g/kg maintenance dose 1g/kg	In divided doses over 2-5 days Every 3 weeks over 1-2 days
Multifocal Motor Neuropathy (MMN)	starting dose: 2 g/kg maintenance dose: 1 g/kg or 2 g/kg	given over 2-5 days every 2-4 weeks or every 4-8 weeks over 2-5 days

d = day