Package leaflet: Information for the user

Nanogam 100 mg/ml solution for infusion
Human normal immunoglobulin (IVIg)

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:

1. What Nanogam is and what it is used for

Nanogam is a solution for infusion that contains immunoglobulins. Immunoglobulins are also known as antibodies and are normal constituents of human blood. Antibodies help your body fight infections. Nanogam is used to raise antibody levels in your blood when the antibody level is too low or if you need additional antibodies in certain diseases. The administration of antibodies can also have an effect in patients with certain inflammatory disorders (autoimmune diseases).

Nanogam is used for:

Replacement therapy (Treatment of patients who do not have sufficient antibodies) in adults, and children and adolescents (0-18 years) in:

- Patients who are born with a reduced ability or inability to produce immunoglobulins (primary immunodeficiency syndromes).
- Patients who have had a disease or treatment that has resulted in a proven lack of immunoglobulin production and who suffer from severe or recurrent infections that do not respond to antimicrobial treatment (secondary immunodeficiency syndromes).

Immunomodulation (Treatment of patients with certain inflammatory disorders) in adults, and children and adolescents (0-18 years) in:

- 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.
- Patients with Guillain Barré syndrome, an acute disease characterised by inflammation of the peripheral nerves that causes serious limb muscle paralysis.
- Patients with Kawasaki disease, a very rare acute disease that primarily affects young children, characterised by inflammation of the blood vessels in the body.
- Patients with chronic inflammatory demyelinating polyradiculoneuropathy, a rare inflammatory disease affecting the peripheral nerves. It causes slowly evolving muscle weakness and numbness of the limbs.
- Patients with multifocal motor neuropathy, a rare autoimmune disorder of the motor nerves resulting in progressive asymmetrical weakness of the limbs.

2. What you need to know before you use Nanogam

Read this section carefully. The information given should be taken into consideration by you and your doctor before you are given Nanogam.

Do not use Nanogam:

- if you are allergic to immunoglobulins or any of the other ingredients of this medicine (listed in section 6). Patients with allergy to corn might also be sensitive to glucose which is an ingredient of Nanogam.
- if you have immunoglobulin A (IgA) deficiency with antibodies against IgA. Nanogam contains a small amount of IgA which might cause an allergic reaction.
- if you have diabetes that is not adequately treated, allowing your blood sugar levels to rise above normal (uncompensated diabetes)
- if you experience states of glucose intolerance, for example when the body's metabolism does not function correctly, e.g. due to severe illness (metabolic stress)
- if you are suffering from a hyperosmolar coma (unconsciousness). This is a type of coma that can occur if you have diabetes and do not receive enough medicine.
- if you have a higher amount of sugar in the blood than normal (hyperglycemia)
- if you have a higher level of lactate in the blood than normal (hyperlactatemia)

Warnings and precautions

Allergic reactions are rare, but may occur even if you have previously received human immunoglobulins and had tolerated them well. If an allergic reaction occurs, administration of Nanogam should be discontinued immediately. If you experience a severe hypersensitivity reaction please tell your doctor of healthcare professional immediately. See also section 4 Possible side effects.

If you experience severe difficulty breathing with increased body temperature within 1 to 6 hours after receiving treatment please tell your doctor of healthcare professional immediately. This could indicate transfusion-related acute lung injury (TRALI). TRALI can occur in very rare cases after receiving immunoglobulins. See also section 4 Possible side effects.

You will be observed carefully during the infusion period and for at least 20 minutes after administration to detect potential adverse reactions (unwanted side effects). Certain adverse reactions may be related to the rate of infusion. Therefore your doctor should make sure that the infusion rate is suitable for you. If you experience a reaction during or after infusion, tell your doctor immediately. The doctor will decide if the infusion should be discontinued.

In certain circumstances special precautions may be necessary, because of an increased risk of adverse reactions. In the following cases you should be monitored in a hospital during infusion and for the first hour after the infusion:

- if you receive Nanogam for the first time
- when the human normal immunoglobulin product is replaced by another product or there has been a long interval since the previous infusion.
- if you have an untreated infection or underlying chronic inflammation.

Nanogam must not be given through the same infusion equipment as a blood transfusion.

Risk factors during treatment with Nanogam

Please tell your doctor if any of the following factors applies to you, since these might be risk factors during the treatment with Nanogam. In particular, tell your doctor if you have:

- or have previously had problems with your kidneys (renal insufficiency)
- medication that may harm your kidneys
- heart-, liver- or kidney diseases or if you use drugs that affects the reabsorption of water in the kidneys (the vasopressin effect)
- certain diuretic medication (called loop diuretics)

- diabetes (abnormally high glucose levels in the blood). Nanogam contains 50 mg of glucose per ml and this may affect your blood sugar level
- history of vascular (blood vessel) diseases or thrombosis (formation of a clot inside a blood vessel)
- hypertension
- overweight
- diseases which increase blood viscosity (thickness of the blood)
- hypovolemia (a decrease in circulating blood volume)
- advanced age (over 65)
- sepsis, traumatic brain injury or shock
- had head injury within the past 24 hours
- had a stroke recently. High levels of sugar in the blood can worsen the effects of stroke and recovery.
- metabolic disturbances due to starvation or malnutrition
- a low level of thiamine (vitamin B1) in your body. This can happen if you for example suffer from chronic alcoholism

While using Nanogam the following should be taken into account

- it is important to make sure that you are adequately hydrated before infusion of Nanogam
- it is important to make sure that there is adequate urine production
- it may be necessary to check your serum creatinine levels (a substance which is an indicator of the activity of the kidneys)
- blood glucose and/or electrolytes may need to be monitored. This is especially the case if you use drugs that increase the vasopressin effect.

Effects on blood tests

If you will have blood tests taken, please tell you doctor that you are using Nanogam, since Nanogam contains antibodies and this may result in misleading positive results in antibody tests.

Other medicines and Nanogam

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

Vaccination

Tell your doctor if you have planned to take a vaccination or have recently taken a vaccination. Nanogam may impair the efficacy of certain live virus vaccines such as measles, rubella, mumps and chickenpox (varicella). After using Nanogam, an interval of three months should elapse before vaccination with these vaccines. In case of measles, you may have to wait up to 1 year.

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.

In pregnant or breast-feeding women the safety of this medicine has not been investigated. However, immunoglobulins have been used in pregnant women and women who are breast-feeding. This experience with immunoglobulins indicates that no harmful effects are expected on the course of a pregnancy nor on the foetus (unborn child) or the newborn.

Clinical experience with immunoglobulins also suggests that no harmful effects on fertility are expected.

If you are breast-feeding and receive Nanogam, the immunoglobulins of the medicine can also be found in the breast milk. No negative effects on the breastfed newborns/infants are anticipated.

Newborns

Newborns – especially those born premature and with low birth weight – are at increased risk of developing a too low or too high level of sugar in the blood (hypo- or hyperglycaemia) and therefore need close

monitoring during treatment with Nanogam to ensure adequate control of the sugar levels in order to avoid potential long term adverse effects.

Driving and using machines

The ability to drive and operate machines may be impaired by some adverse reactions associated with Nanogam. Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

Nanogam contains glucose

Nanogam contains 50 mg glucose per ml (5%). Please note that this may increase your blood glucose levels. If you are a diabetic, your doctor will decide if there is a need to monitor your blood glucose levels and a need for insulin, especially if high doses of Nanogam are given.

Information on viral safety of Nanogam

Nanogam is made from human plasma. When medicines are made from human blood or plasma, certain 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
- the testing of each donation and pools of plasma for signs of virus/infections
- 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 are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped viruses such as hepatitis A virus and parvovirus B19.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

Batch number control:

It is strongly recommended that every time you receive a dose of Nanogam the name and batch number of the product are recorded in order to maintain a record of the batches used.

3. How to use Nanogam

Nanogam is given to you by your doctor or nurse. Nanogam may be self-administered if it is an approved practice in your country and when you have been trained sufficiently. Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Bring Nanogam to room or body temperature before use. Start the intravenous infusion of Nanogam as soon as possible after puncturing the stopper.

The solution should be clear or slightly opalescent and colourless or pale yellow. Do not use solutions that are cloudy or have deposits. Discard any unused solution.

Dosage and route of administration

Nanogam is intended for infusion into a vein (intravenous infusion). The dose and frequency of infusion will vary depending on your condition and body weight. At the beginning of your infusion, you will receive Nanogam at a slow rate. Dependent how comfortable you are, your doctor may gradually increase the infusion rate. If your administer Nanogam yourself your doctor will tell you the dose and infusion rate.

Use in children and adolescents

For children and adolescents the same indications, dose and frequencies of infusion apply as for adults.

If you use more Nanogam than you should

If you receive more Nanogam than you should, there is a risk of fluid overload and your blood may become too thick (hyperviscous), which may increase the risk of blood clots. This could particularly happen when you are a patient at risk, e.g. an elderly patient or if your kidneys are not working well or if you have cardiac problems. Tell your doctor if you are known to have medical problems.

If you forget to use Nanogam

Tell your doctor immediately and follow his/her instructions. Do not take a double dose to make up for a forgotten dose.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop the infusion and contact your doctor immediately if you experience any of the following side effects:
- allergic reactions with symptoms such as a sudden fall in blood pressure, severe dizziness, and swelling of your lips, tongue or throat, itching, hives and difficulty breathing (rare side effect)
- pain in the chest or one of your legs, which might be caused by heart attack (myocardial infarction), stroke, blood clots in the lung (lung embolism), or blood clots in a blood vessel in the leg (deep vein thromboses) (very rare side effect)
- severe difficulty breathing with increased body temperature within 1 to 6 hours after receiving treatment, which may be due to transfusion related acute lung injusry (TRALI) (see also section 2) (very rare side effect)

Other side effects that may be caused by human normal immunoglobulins are:
- meningitis without infection (aseptic meningitis)
- increased serum creatinine level and/or acute kidney failure
- disruption of red cells (haemolytic reactions, haemolytic anaemia)
- vomiting, joint pain (arthralgia)

Other side effects reported for Nanogam are:
Uncommon side effects (may occur in up to 1 in 100 infusions):
- Hypersensitivity reactions
- Headache
- Nausea
- Skin disorders (such as rash, redness (erythema), hives (urticaria), itching (pruritus), blister, skin peeling (exfoliation))
- Back pain, neck pain, muscle pain (myalgia)
- Malaise (i.e. fatigue, chills, fever, flu-like illness)

Rare side effects (may occur in up to 1 in 1,000 infusions):
- Low white blood cell count in the blood (leukopenia, neutropenia)
- Migraine
- Dizziness
- Throbbing heartbeat (palpitations), fast heart beat (tachycardia)
- High blood pressure (hypertension), low blood pressure (hypotension)
- Shortness of breath (dyspnoea)
- Diarrhoea
- Profuse sweating (hyperhidrosis)

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 <Dutch pharmacovigilance centre LAREB, Website: www.lareb.nl>. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Nanogam

Keep this medicine out of the sight and reach of children.

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect it from light.

Nanogam can be stored at or below 25°C up to six months, for example while travelling, without impairing its efficacy. The date when taken to room temperature should be marked on the package. If not used during six months storage at room temperature the product must be discarded.

Do not use this medicine after the expiry date which is stated on the label and the carton after EXP. The expiry date refers to the last day of that month.

Do not use this medicine if the solution is cloudy or you notice particles floating in the solution.

6. Contents of the pack and other information

What Nanogam contains

- The active substance is human normal immunoglobulin for intravenous administration. One ml contains 100 mg immunoglobulin, of which at least 95% is immunoglobulin G (IgG).
- The other ingredients are glucose (as glucose monohydrate) and water for injections.

What Nanogam looks like and contents of the pack

Nanogam is a solution for infusion. The solution is clear or slightly opalescent and colourless or pale yellow.

Nanogam is supplied in the following pack sizes:

10 ml of solution in a vial containing 1 g of human normal immunoglobulin,
25 ml of solution in a vial containing 2.5 g of human normal immunoglobulin,
50 ml of solution in a vial containing 5 g of human normal immunoglobulin,
100 ml of solution in a vial containing 10 g of human normal immunoglobulin,
200 ml of solution in a vial containing 20 g of human normal immunoglobulin,
300 ml of solution in a vial containing 30 g of human normal immunoglobulin.

Not all sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Prothya Biosolutions Netherlands B.V.
Plesmanlaan 125
NL-1066 CX Amsterdam
The Netherlands

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Germany: Optiglobin 100 mg/ml Infusionslösung
Belgium, Netherlands: Nanogam 100 mg/ml oplossing voor infusie
Cyprus: Nanogam 100 mg/ml διάλυμα για έγχυση
Fínland: Nanogam 100 mg/ml infuusioneste, liuos
Poland: Optiglobin 100 mg/ml, Roztwór do infuzji
Slovakia: Nanogam 100 mg/ml, Infúzny roztok

Sweden: Nanogam 100 mg/ml, Infusionsvätska, lösning

This leaflet was last revised in October 2021

The following information is intended for medicinal or healthcare professionals only:

Posology and method of administration

Nanogam must only be administered intravenously.

Start the intravenous infusion of Nanogam as soon as possible after puncturing the stopper. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user. The in-use storage times would normally not be longer than 24 hours at 2°C – 8°C, unless puncturing has taken place in controlled and validated aseptic conditions.

If you need large quantities of Nanogam, it is also possible to transfer the contents of several vials to a single Ethyl Vinyl Acetate container (Clintec® EVA-parenteral nutrition container, Baxter, CE0123). These containers can be filled with Nanogam at a minimum of 20% up to a maximum of 80% of the total container volume for 500 ml and 1 L containers. Use an aseptic technique for all the steps. For microbiological reasons, start the infusion as soon as possible after transfer of Nanogam into the EVA-container, but not later than 3 hours after the transfer.

The dose and dosage depend on the indication.

Nanogam is given as an intravenous infusion under controlled circumstances at an initial rate of 0.5 ml/kg/hr for 20 minutes. If well tolerated, the rate of administration may gradually be increased to 1.0 ml/kg/hr for 20 minutes and thereafter increased to a maximum of 3.0 ml/kg/hr for the first time users. In adult patients who receive Nanogam on a regular base with good tolerance, the infusion rate of repeat infusions may be started at the last well-tolerated infusion rate or lower. If well tolerated, the rate of administration of regular Nanogam users may gradually be increased by 1.0 ml/kg/hr every 20 minutes up to a maximum of 7.0 ml/kg/hr.

The dose and dosage regimen is dependent on the indication. The dose may need to be individualised for each patient dependent on the clinical response. Dose based on bodyweight may require adjustment in underweight or overweight patients.

In replacement therapy the dosage may need to be individualized for each patient dependent on the pharmacokinetic and clinical response.

The dosage recommendations are summarised in the following table:

Indication	**Dose**	**Frequency of injections**
REPLACEMENT THERAPY		
Primary immunodeficiency syndromes	Starting dose: 0.4 - 0.8 g/kg Maintenance dose: 0.2-0.8 g/kg	 every 3-4 weeks
Secondary immunodeficiencies	0.2-0.4 g/kg	every 3-4 weeks
IMMUNOMODULATION		
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 1 dose in association with acetylsalicylic acid
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	Starting dose: 2 g/kg Maintenance dose: 1 g/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	over 2-5 consecutive days every 2-4 weeks or every 4-8 weeks over 2-5 days

Special precautions

In case of an adverse reaction, either the rate of administration must be reduced or the infusion stopped.

It is strongly recommended that every time you receive a dose of Nanogam the name and batch number of the product are recorded in order to maintain a record of the batches used.

Incompatibilities

Nanogam should not be mixed with other medicines.

Instructions for handling and disposal

Bring Nanogam to room or body temperature before use.

The solution should be clear or slightly opalescent and colourless or pale yellow. Do not use solutions that are cloudy or have deposits.

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