PACKAGE LEAFLET

Package leaflet: Information for the user

Nanogam 50 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 or pharmacist.
- 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 contains human normal immunoglobulins (also called antibodies). Immunoglobulins are normal constituents of human blood which help the body fight infections. Nanogam is used to raise antibody levels in the blood when the antibody level is too low or if you need additional antibodies in certain diseases (e.g. immune-mediated diseases).

Nanogam is used in adults, children and adolescents (0-18 years) in the following situations:

Replacement therapy to increase low immunoglobulin levels to normal in patients:

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

Immunomodulation to treat certain immune-mediated disorders 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.
- with Guillain Barré syndrome, an acute disease characterised by inflammation of the peripheral nerves that causes severe muscle weakness of the limbs.
- with Kawasaki disease, an acute disease that primarily affects young children, characterised by inflammation of the blood vessels in the body.
- with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), an immune-mediated disease affecting the peripheral nerves and causing slowly evolving muscle weakness and numbness of the limbs.
- with multifocal motor neuropathy (MMN), an immune-mediated 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 in these persons.
- if you have diabetes that is not adequately treated and your blood sugar exceeds normal levels (uncompensated diabetes).
- if you experience states of glucose intolerance.
- if you recently suffered a hyperosmolar coma (unconsciousness due to very high blood sugar that leads to severe dehydration and highly concentrated blood (high osmolality)).
- if you have high blood glucose levels (hyperglycemia) due to causes other than diabetes.
- if you have high blood lactic acid levels (hyperlactatemia).

Warnings and precautions

In order to improve the traceability of biological medicinal products, the name and the batch number (stated on the vial label and carton after Lot) of the administered product should be clearly recorded.

Talk to your doctor or pharmacist before using Nanogam.

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 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.

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 allergic reaction, tell your doctor or other 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, tell your doctor or other 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.

Risk factors during treatment with Nanogam

Tell your doctor or other healthcare professional if any of the following factors apply to you, since these might be risk factors during the treatment with Nanogam. In particular, tell your healthcare professional if you:

- have or have previously had problems with your kidneys (renal insufficiency).
- take medication that may harm your kidneys.
- have heart-, liver- or kidney diseases or if you use drugs that affects the reabsorption of water in the kidneys (the vasopressin effect).
- take certain diuretic medication (called loop diuretics).
- have diabetes (abnormally high glucose levels in the blood). Nanogam contains 50 mg of glucose per ml and this may affect your blood sugar level.
- have a history of vascular (blood vessel) diseases or thrombosis (formation of a clot inside a blood vessel).
- have a high blood pressure.
- are overweight.
- have a disease which increases blood viscosity (thickness of the blood).
- have hypovolemia (a decrease in circulating blood volume).
- have an advanced age (over 65 years).
- have any signs of sepsis, traumatic brain injury or shock.
- have had head injury within the past 24 hours.
- had a stroke recently (Nanogam contains glucose, blood sugar levels might increase and thus worsen the stroke effects on the brain and its recovery).
- have metabolic disturbances due to starvation or malnutrition.
- have a low level of thiamine (vitamin B1) in your body.

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 and 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, tell your healthcare professional that you are using Nanogam, as antibodies within the Nanogam solution may result in misleading positive results in antibody tests.

Other medicines and Nanogam

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 get a vaccination or have recently had 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.

Based on the clinical experience with immunoglobulins, no harmful effects are expected on fertility, nor on the course of a pregnancy nor on the foetus (unborn child) or the newborn. When Nanogam is administered

to pregnant women during labour, particularly if administered in combination with oxytocin, there may be an increased risk for hyponatraemia (low sodium levels in the blood).

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% glucose) which may increase 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, and
- the inclusion of 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.

3. How to use Nanogam

Nanogam is given to you by your doctor or an other healthcare professional. 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 immediately 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 bodyweight. At the beginning of your infusion, you will receive Nanogam at a slow rate. If well tolerated, your doctor may gradually increase the infusion rate. If you administer Nanogam yourself, your doctor will tell you the dose and infusion rate.

Use in children and adolescents

For children and adolescents (0-18 years) 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 or the healthcare professional if you are known to have such medical problems.

If you forget to use Nanogam

Tell your doctor or the healthcare professional 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 or the healthcare professional 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, shortness of breath, or pain in one of your legs, or severe headache. These symptoms 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 thrombosis) (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 injury (TRALI) (see also section 2) (very rare side effect).

Other side effects that may be caused by human normal immunoglobulins are:
- inflammation (swelling) of the protective membranes covering the brain and spinal cord not caused by bacteria (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, hives, itching, blister, skin peeling), back pain, neck pain, muscle pain, 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, fast heartbeat, high blood pressure, low blood pressure, shortness of breath, diarrhoea, profuse sweating.

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.

Within its shelf life, Nanogam may be stored at or below 25 °C for up to six months without being refrigerated again. If not used within this period, it must be discarded. Indicate the date on the outer carton when it was brought to room temperature.

Do not use this medicine after the expiry date which is stated on the vial 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 if you notice particles floating in the solution.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Nanogam contains

- The active substance is human normal immunoglobulin for intravenous administration. One ml contains 50 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.

Pack sizes: 1 vial of 1 g/20 ml, 2.5 g/50 ml, 5 g/100 ml, 10 g/200 ml or 20 g/400 ml. Not all pack 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:

Finland, Netherlands: Nanogam 50 mg/ml, solution for infusion

This leaflet was last revised in February 2025.

The following information is intended for healthcare professionals only:

Posology and method of administration

Nanogam must only be administered intravenously.

From a microbiological point of view, the product should be used immediately after puncturing the rubber stopper. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C – 8 °C, unless puncturing has taken place in controlled and validated aseptic conditions.

For patients receiving 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.

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.

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Incompatibilities

Nanogam should not be mixed with other medicines.

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

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.