

Package leaflet: Information for the user

Neupogen® 30 MU (0.6 mg/ml) Neupogen® 48 MU (0.96 mg/ml) solution for injection in a pre-filled syringe filgrastim

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, nurse 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 Neupogen is and what it is used for
2. What you need to know before you use Neupogen
3. How to use Neupogen
4. Possible side effects
5. How to store Neupogen
6. Contents of the pack and other information
7. Instructions for injecting Neupogen

1. What Neupogen is and what it is used for

Neupogen is a white blood cell growth factor (granulocyte colony stimulating factor) and belong to a group of medicines called cytokines. Growth factors are proteins that are produced naturally in the body but they can also be made using biotechnology for use as a medicine. Neupogen works by encouraging the bone marrow to produce more white blood cells.

A reduction in the number of white blood cells (neutropenia) can occur for several reasons and makes your body less able to fight infection. Neupogen stimulates the bone marrow to produce new white cells quickly.

Neupogen can be used:

- to increase the number of white blood cells after treatment with chemotherapy to help prevent infections;
- to increase the number of white blood cells after a bone marrow transplant to help prevent infections;
- before high-dose chemotherapy to make the bone marrow produce more stem cells which can be collected and given back to you after your treatment. These can be taken from you or from a donor. The stem cells will then go back into the bone marrow and produce blood cells;
- to increase the number of white blood cells if you suffer from severe chronic neutropenia to help prevent infections;
- in patients with advanced HIV infection which will help reduce the risk of infections.

2. What you need to know before you use Neupogen

Do not use Neupogen

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

Warnings and precautions

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

Please tell your doctor before starting treatment **if you have:**

- sickle cell anaemia, as Neupogen may cause sickle cell crisis.
- an allergy to natural rubber (latex). The needle cover on the syringe may be made from a type of natural rubber and may cause allergic reactions.
- osteoporosis (bone disease).

Please tell your doctor immediately during treatment with Neupogen, if you:

- have sudden signs of allergy such as rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or trouble breathing as these could be signs of a severe allergic reaction (hypersensitivity).
- experience puffiness in your face or ankles, blood in your urine or brown-coloured urine or you notice you urinate less than usual (glomerulonephritis).
- get left upper belly (abdominal) pain, pain below the left rib cage or at the tip of your left shoulder (these may be symptoms of an enlarged spleen (splenomegaly), or possibly rupture of the spleen).
- notice unusual bleeding or bruising (these may be symptoms of a decrease in blood platelets (thrombocytopenia), with a reduced ability of your blood to clot).
- inflammation of aorta (the large blood vessel which transports blood from the heart to the body) has been reported rarely in cancer patients and healthy donors. The symptoms can include fever, abdominal pain, malaise, back pain and increased inflammatory markers. Tell your doctor if you experience those symptoms.

Loss of response to filgrastim

If you experience a loss of response or failure to maintain a response with filgrastim treatment, your doctor will investigate the reasons why including whether you have developed antibodies which neutralise filgrastim's activity.

Your doctor may want to monitor you closely, see section 4 of the package leaflet.

If you are a patient with severe chronic neutropenia, you may be at risk of developing cancer of the blood (leukaemia, myelodysplastic syndrome (MDS)). You should talk to your doctor about your risks of developing cancers of the blood and what testing should be done. If you develop or are likely to develop cancers of the blood, you should not use Neupogen, unless instructed by your doctor.

If you are a stem cell donor, you must be aged between 16 and 60 years.

Take special care with other products that stimulate white blood cells

Neupogen is one of a group of products that stimulate the production of white blood cells. Your healthcare professional should always record the exact product you are using.

Other medicines and Neupogen

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

Pregnancy and breast-feeding

Neupogen has not been tested in pregnant or breast-feeding women.

Neupogen is not recommended during pregnancy.

It is important to tell your doctor if you:

- are pregnant or breast-feeding;
- think you may be pregnant; or
- are planning to have a baby.

Unless your doctor directs you otherwise, you must stop breast-feeding if you use Neupogen.

Driving and using machines

Neupogen may have a minor influence on your ability to drive and use machines. This medicine may cause dizziness. It is advisable to wait and see how you feel after taking Neupogen and before driving or operating machinery.

Neupogen contains sodium

Neupogen contains less than 1 mmol (23 mg) sodium per 0.6 mg/ml or 0.96 mg/ml dose, that is to say essentially 'sodium free'.

Neupogen contains sorbitol

This medicine contains 50 mg sorbitol in each ml.

Sorbitol is a source of fructose. If you (or your child) have hereditary fructose intolerance (HFI), a rare genetic disorder, you (or your child) must not receive this medicine. Patients with HFI cannot break down fructose, which may cause serious side effects.

You must tell your doctor before receiving this medicine if you (or your child) have HFI or if your child can no longer take sweet foods or drinks because they feel sick, vomit or get unpleasant effects such as bloating, stomach cramps or diarrhoea.

3. How to use Neupogen

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

How is Neupogen given and how much should I take?

Neupogen is usually given as a daily injection into the tissue just under the skin (known as a subcutaneous injection). It can also be given as a daily slow injection into the vein (known as an intravenous infusion). The usual dose varies depending on your illness and weight. Your doctor will tell you how much Neupogen you should take.

Patients having a bone marrow transplant after chemotherapy:

You will normally receive your first dose of Neupogen at least 24 hours after your chemotherapy and at least 24 hours after receiving your bone marrow transplant.

You, or people caring for you, can be taught how to give subcutaneous injections so that you can continue your treatment at home. However, you should not attempt this unless you have been properly trained first by your health care provider.

How long will I have to take Neupogen?

You will need to take Neupogen until your white blood cell count is normal. Regular blood tests will be taken to monitor the number of white blood cells in your body. Your doctor will tell you how long you will need to take Neupogen.

Use in children

Neupogen is used to treat children who are receiving chemotherapy or who suffer from severe low white blood cell count (neutropenia). The dosing in children receiving chemotherapy is the same as for adults.

If you use more Neupogen than you should

Do not increase the dose your doctor has given you. If you think you have injected more than you should, contact your doctor as soon as possible.

If you forget to use Neupogen

If you have missed an injection, or injected too little, contact your doctor as soon as possible. Do not take a double dose to make up for any missed doses.

If you have any further questions on the use of this product, ask your doctor, nurse or pharmacist.

4. Possible side effects

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

Please tell your doctor immediately during treatment:

- if you experience an allergic reaction including weakness, drop in blood pressure, difficulty breathing, swelling of the face (anaphylaxis), skin rash, itchy rash (urticaria), swelling of the face lips, mouth, tongue or throat (angioedema) and shortness of breath (dyspnoea).
- if you experience a cough, fever and difficulty breathing (dyspnoea) as this can be a sign of Acute Respiratory Distress Syndrome (ARDS).
- if you experience kidney injury (glomerulonephritis). Kidney injury has been seen in patients who received Neupogen. Call your doctor right away if you experience puffiness in your face or ankles, blood in your urine or brown-coloured urine or you notice you urinate less than usual.
- if you have any of the following or combination of the following side effects:
 - swelling or puffiness, which may be associated with passing water less frequently, difficulty breathing, abdominal swelling and feeling of fullness, and a general feeling of tiredness. These symptoms generally develop in a rapid fashion.These could be symptoms of a condition called “Capillary Leak Syndrome” which causes blood to leak from the small blood vessels into your body and needs urgent medical attention.
- if you have a combination of any of the following symptoms:
 - fever, or shivering, or feeling very cold, high heart rate, confusion or disorientation, shortness of breath, extreme pain or discomfort and clammy or sweaty skin.These could be symptoms of a condition called “sepsis” (also called "blood poisoning"), a severe infection with whole-body inflammatory response which can be life-threatening and needs urgent medical attention.
- if you get left upper belly (abdominal) pain, pain below the left rib cage or pain at the tip of your shoulder, as there may be a problem with your spleen (enlargement of the spleen (splenomegaly) or rupture of the spleen).
- if you are being treated for severe chronic neutropenia and you have blood in your urine (haematuria). Your doctor may regularly test your urine if you experience this side effect or if protein is found in your urine (proteinuria).

A common side effect of Neupogen use is pain in your muscles or bones (musculoskeletal pain), which can be helped by taking standard pain relief medicines (analgesics). In patients undergoing a stem cell or bone marrow transplant, Graft versus host disease (GvHD) may occur- this is a reaction of the donor cells against the patient receiving the transplant; signs and symptoms include rash on the palms of your hands or soles of your feet and ulcer and sores in your mouth, gut, liver, skin, or your eyes, lungs, vagina and joints.

In normal stem cell donors an increase in white blood cells (leukocytosis) and a decrease of platelets may be seen this reduces the ability of your blood to clot (thrombocytopenia), these will be monitored by your doctor.

Very common side effects (may affect more than 1 in 10 people):

- decrease of platelets which reduces the ability of blood to clot (thrombocytopenia)
- low red blood cell count (anaemia)
- headache
- diarrhoea
- vomiting
- nausea
- unusual hair loss or thinning (alopecia)
- tiredness (fatigue)
- soreness and swelling of the digestive tract lining which runs from the mouth to the anus (mucosal inflammation)
- fever (pyrexia)

Common side effects (may affect up to 1 in 10 people):

- inflammation of the lung (bronchitis)
- upper respiratory tract infection
- urinary tract infection
- decreased appetite
- trouble sleeping (insomnia)
- dizziness
- decreased feeling of sensitivity, especially in the skin (hypoesthesia)
- tingling or numbness of the hands or feet (paraesthesia)
- low blood pressure (hypotension)
- high blood pressure (hypertension)
- cough
- coughing up blood (haemoptysis)
- pain in your mouth and throat (oropharyngeal pain)
- nose bleeds (epistaxis)
- constipation
- oral pain
- enlargement of the liver (hepatomegaly)
- rash
- redness of the skin (erythema)
- muscle spasm
- pain when passing urine (dysuria)
- chest pain
- pain
- generalised weakness (asthenia)
- generally feeling unwell (malaise)
- swelling in the hands and feet (oedema peripheral)
- increase of certain enzymes in the blood
- changes in blood chemistry
- transfusion reaction

Uncommon side effects (may affect up to 1 in 100 people):

- increase in white blood cells (leukocytosis)
- allergic reaction (hypersensitivity)
- rejection of transplanted bone marrow (graft versus host disease)
- high uric acid levels in the blood, which may cause gout (hyperuricaemia) (blood uric acid increased)
- liver damage caused by blocking of the small veins within the liver (veno-occlusive disease)
- lungs do not function as they should, causing breathlessness (respiratory failure)
- swelling and/or fluid in the lungs (pulmonary oedema)
- inflammation of the lungs (interstitial lung disease)
- abnormal x-rays of the lungs (lung infiltration)
- bleeding from the lung (pulmonary haemorrhage)
- lack of absorption of oxygen in the lung (hypoxia)
- bumpy skin rash (rash maculo-papular)
- disease which causes bones to become less dense, making them weaker, more brittle and likely to break (osteoporosis)
- injection site reaction

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Neupogen

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

Store in a refrigerator (2°C – 8°C).

Keep the container in the outer carton in order to protect from light.

Accidental freezing will not harm Neupogen.

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

Do not use this medicine if you notice discolouration, cloudiness or particles, it should be a clear, colourless liquid.

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

6. Contents of the pack and other information

What Neupogen contains

- The active substance is filgrastim 30 million units (0.6 mg/ml) or 48 million units (0.96 mg/ml).
- The other ingredients are sodium acetate, sorbitol (E420), polysorbate 80, water for injections.

What Neupogen looks like and contents of the pack

Neupogen is a clear colourless solution for injection (injection)/concentrate for solution for infusion (sterile concentrate) in a pre-filled syringe.

Neupogen is available in packs of one or five pre-filled syringes. Not all pack sizes may be marketed.

Site of Manufacture of the Drug Product

Amgen Manufacturing Limited
State Road 31
Kilometer 24.6
Juncos 00777-4060
Puerto Rico
USA

Marketing Authorisation Holder and Manufacturer

Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

This leaflet was last revised in March 2019.

THIS MEDICINE

Is a product, which affects your health, and its consumption contrary to instructions is dangerous for you.

Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicine.

- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.

7. Instructions for injecting Neupogen

This section contains information on how to give an injection of Neupogen.

Important: do not try to give yourself an injection unless you have received training from your doctor or nurse.

Neupogen is injected into the tissue just under the skin. This is known as a subcutaneous injection.

Equipment that you need

To give yourself a subcutaneous injection you will need:

- a new pre-filled syringe of Neupogen; and
- alcohol wipes or similar.

What do I do before I give myself a subcutaneous injection of Neupogen?

1. Remove one tray containing a syringe from the refrigerator and leave at room temperature for approximately 30 minutes, or hold gently in your hand for a few minutes. This will make the

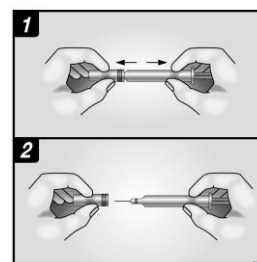
injection more comfortable. **Do not** warm Neupogen in any other way (for example, do not warm it in a microwave or in hot water).

2. Do not shake the pre-filled syringe.
3. Place the tray in your hand and peel the paper off the tray.
4. Flip the tray to place the pre-filled syringe onto your palm.
5. **Do not** remove the needle cover until you are ready to inject.
6. Check the expiry date on the pre-filled syringe label (EXP). Do not use it if the date has passed the last day of the month shown.
7. Check the appearance of Neupogen. It must be a clear and colourless liquid. If there is discolouration, cloudiness or particles in it, you must not use it.
8. **Wash your hands thoroughly.**
9. Find a comfortable, well-lit, clean surface and put all the equipment you need within reach.

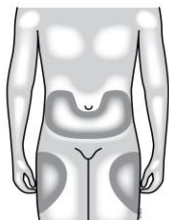
How do I prepare my Neupogen injection?

Before you inject Neupogen you must do the following:

1. To avoid bending the needle, securely grasp the pre-filled syringe by the glass barrel. Gently pull the cover from the needle without twisting as shown in pictures 1 and 2.
2. Do not touch the needle or push the plunger.
3. You may notice a small air bubble in the pre-filled syringe. You do not have to remove the air bubble before injecting. Injecting the solution with the air bubble is harmless.
4. You can now use the pre-filled syringe.



Where do I give my injection?



The best places to inject are the top of your thighs and the abdomen. If someone else is injecting you, they can also use the back of your arms.

You may change the injection site if you notice the area is red or sore.

How do I give my injection?

1. Disinfect your skin by using an alcohol wipe and pinch (without squeezing) the skin between your thumb and forefinger.
2. Put the needle fully into the skin as shown by your nurse or doctor.
3. Push the plunger with a slow constant pressure, always keeping your skin pinched, until the syringe is empty.
4. Remove the needle and let go of your skin.
5. If you notice a spot of blood you may gently dab it away with a cotton ball or tissue. Do not rub the injection site. If needed, you may cover the injection site with a plaster.
6. Only use each syringe for one injection. Do not use any Neupogen that may be left in the syringe.

Remember: if you have any problems, please do not be afraid to ask your doctor or nurse for help and advice.

Disposing of used syringes

- Do not put the cover back on used needles, as you may accidentally prick yourself.
- Keep used syringes out of the reach and sight of children.
- Syringes should not be thrown out in the household rubbish. Your pharmacist will know how to dispose of used syringes or syringes no longer needed.

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

When being used as a concentrate for solution for infusion, Neupogen should be diluted in 20 ml of 5% glucose solution. Please see the Summary of Product Characteristics for full details.

Rare side effects (may affect up to 1 in 1,000 people):

- severe pain in the bones, chest, gut or joints (sickle cell anaemia with crisis)
- sudden life-threatening allergic reaction (anaphylactic reaction)
- pain and swelling of the joints, similar to gout (pseudogout)
- a change in how your body regulates fluids within your body and may result in puffiness (fluid volume disturbances)
- inflammation of the blood vessels in the skin (cutaneous vasculitis)
- plum-coloured, raised, painful sores on the limbs and sometimes the face and neck with a fever (Sweets syndrome)
- worsening of rheumatoid arthritis
- unusual change in the urine
- bone density decreased
- Inflammation of aorta (the large blood vessel which transports blood from the heart to the body), see section 2