Package leaflet: Information for the patient

GRANOCYTE 13 million IU/mL, powder and solvent for solution for injection/infusion in a pre-filled syringe
GRANOCYTE 34 million IU/mL, powder and solvent for solution for injection/infusion in a pre-filled syringe
Lenograstim

Read all of this leaflet carefully before you start taking 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Granocyte is and what it is used for

The name of your medicine is Granocyte, powder and solvent for injection/infusion (called Granocyte in this leaflet). Granocyte contains a medicine called lenograstim. This belongs to a group of medicines called cytokines.

Granocyte works by helping your body to make more of the blood cells which fight infection.
- These blood cells are made in your bone marrow.
- Granocyte encourages your bone marrow to make more cells called 'blood stem cells'.
- It then helps turn these young blood cells into fully working blood cells.
- In particular, it helps produce more white blood cells called neutrophils. Neutrophils are important in fighting infections.

Granocyte is used:
- **After cancer treatment, if the level of your white blood cells is too low (called 'neutropenia')**
  Some treatments for cancer (also called 'chemotherapy') affect the bone marrow. This can lower the number of your white cells. It particularly affects the neutrophils and is called 'neutropenia'. It lasts until your body is able to produce more white blood cells. When you have a low number of neutrophils it is easier to get infections. These can sometimes be very serious. Granocyte will help reduce the time you have low levels of cells. It does this by encouraging your body to make new white blood cells.

• **When you need to increase your own blood stem cells (called 'mobilisation')**
Granocyte can be used to encourage your bone marrow to produce blood stem cells. This is called 'mobilisation'. This can happen alone or possibly after chemotherapy. These blood stem cells are taken out of your blood and collected using a special machine. The blood stem cells can then be stored and given back to you in a transfusion.
• **After a bone marrow or blood stem cell transplant**
When you are going to have a bone marrow or a blood stem cell transplant, you are first given a high dose chemotherapy or total body irradiation. This is to kill your sick cells. A bone marrow or blood stem cell transplant is then given to you as a blood transfusion. It will take some time for your new bone marrow to start producing new blood cells (including the white blood cells). Granocyte will help your body to speed up the recovery of your new white blood cells.
• **When you want to donate your blood stem cells**
Granocyte can also be used in healthy donors. Here they encourage the bone marrow to produce extra blood stem cells. This is called mobilisation - see above. These healthy donors can then donate blood stem cells to someone who needs them.

Granocyte can be used in adults, adolescents, and children older than 2 years.

2. What you need to know before you take Granocyte
Do not take Granocyte:
• if you are allergic to lenograstim or any of the other ingredients of this medicine (listed in section 6). Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
• if you have a type of cancer called 'myeloid cancer'. However, you can have Granocyte if you have newly diagnosed 'acute myeloid leukemia' in certain cases, if you are more than 55 years old.
• if you are having cancer chemo-therapy on the same day.
Do not take this medicine if any of the above apply to you. If you are not sure talk to your doctor or pharmacist before being given Granocyte.

Warnings and precautions
Talk to your doctor or pharmacist before taking this medicine:
• if you have ever had any illness, especially allergies, infections, kidney or liver problems.
• if you have sickle cell disease or sickle cell trait as Granocyte may potentially cause sickle cell crisis.
Please tell your doctor immediately during the treatment of Granocyte, if you:
• Have pain in your upper left side of your tummy or your left shoulder. These could be signs of an increase in the size of your spleen or a possible rupture of the spleen.
• Experience puffiness in your face or ankles, blood in your urine or brown-coloured urine or notice you urinate less than usual
If you are not sure if this applies to you, talk to your doctor or pharmacist before having Granocyte.

During the treatment with lenograstim, your doctor might recommend additional monitoring as some patients have developed blood clots in the veins and arteries (see also section 4 "Possible side effects").

Inflammation of the 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 these symptoms.

Children and adolescents
Talk to your doctor before taking this medicine:
- if you or your child have a type of cancer called "acute lymphocytic leukaemia" and if you or your child are less than 18 years old.

Other medicines and Granocyte
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, including herbal medicines.

If you want to donate your blood stem cells and you are having anti-coagulant treatment (such as warfarin or heparin), make sure the doctor knows this before starting with the Granocyte. Also tell them if you know you have any other blood clotting problems.

If you are given anti-cancer chemotherapy, do not use Granocyte during the period from 24 hours before the therapy starts to 24 hours after the therapy ends.

Pregnancy and breast-feeding
Do not take this medicine if you are pregnant, might become pregnant or are breast-feeding unless your doctor tells you it is necessary. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Granocyte has not been tested in pregnant women or in breast-feeding.

Driving and using machines
The effect of Granocyte on the ability to drive or use machines or tools is not known. Wait to see how Granocyte affects you before driving or using tools or machines.

Granocyte contains phenylalanine.
This medicine contains 10mg phenylalanine (10 mg/mL after reconstitution) in each vial.

Phenylalanine may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

Granocyte contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. How to take Granocyte

Granocyte must be given under supervision at an experienced Oncology or Haematology centre. It will normally be given by a doctor, nurse or pharmacist. It is given in an injection or an infusion.

However, some patients have been taught how to give themselves the injection. If you have any questions about how this medicine is given, speak to your doctor, nurse or pharmacist.

How much Granocyte is given

If you are not sure why you are being given Granocyte or have any questions about how much Granocyte is being given to you, speak to your doctor, nurse or pharmacist.

After a bone marrow transplant, chemotherapy or for mobilisation of blood stem cells after chemotherapy

- Your doctor will work out how much to give you, depending on the surface area of your body. This is worked out using your weight and height. It is measured in 'square metres', which is written as 'm^2'
- The usual dose of Granocyte is 19.2 MIU (150 micrograms) for each m^2 of body surface area each day. The dose in children older than 2 years and adolescent is the same as in adults"
- The number of days you get Granocyte will be decided by your doctor. You may be given it for up to 28 days
- When Granocyte is given for mobilisation of blood stem cells after chemotherapy, your doctor will tell you when the collection of your blood stem cells will happen

For blood stem cell mobilization with Granocyte alone

- Your doctor will work out how much to give you, depending on your weight.
- The usual dose of Granocyte is 1.28 MIU (10 micrograms) for each kg body weight each day. The dose in children older than 2 years and adolescent is the same as in adults"
- You will be given Granocyte as an injection beneath the skin for 4 to 6 days
- Collection of your blood stem cells will happen between 5 and 7 days later.

GRANOCYTE 13 million IU/mL can be used in patients with body surface area up to 0.7 m^2.
GRANOCYTE 34 million IU/mL can be used in patients with body surface area up to 1.8 m^2.

If you take more Granocyte than you should

If you are given this medicine by a doctor, nurse or pharmacist it is unlikely they will give you too much medicine. They will monitor your progress and check the dose. Always ask if you are not sure why you are getting a dose of medicine.

If you give yourself too much Granocyte, tell a doctor or go to the hospital straight away. Take this medicine pack with you. This is so the doctor knows what you have taken. You may get particularly bad side effects if you have too much. The most likely problem you may have is muscle and bone pain.

If you forget to take Granocyte

Do not take a double dose to make up for a forgotten injection. Always speak to your doctor who will tell you what you should do.

Blood tests

A doctor needs to monitor you while you are having this medicine. They will need to do regular blood tests. These will check the level of your different blood cells (neutrophils, other white blood cells, red blood cells, platelets).

Other blood tests which may be taken by other doctors can show changes while you are having Granocyte. If you are having blood tests, it is important to tell the doctor that you are having Granocyte. The number of your white blood cells may go up, the number of your platelets may go down and there may be an increase in enzyme levels. These changes usually improve after you have stopped having Granocyte. If you are having blood tests, it is important to tell the doctor you are having Granocyte.

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

4. Possible side effects

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

For cancer patients and healthy donors:

Stop taking Granocyte and tell your doctor straight away if:

- Pain in your upper left side of your tummy or your left shoulder. These could be signs of an increase in the size of your spleen. This is a common side effect called splenomegaly but a very rare side effect may cause the spleen to split.
- You have a very serious allergic reaction called 'anaphylactic shock'. This is a sudden life-threatening reaction. The signs include feeling faint, weakness, difficulty breathing or swelling of the face. This is a very rare side effect.
- You have breathing problems. The signs include cough, fever or you may easily become out of breath. These can be signs of Acute Respiratory Distress Syndrome (ARDS) which is a very rare side effect.
- 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 an uncommon (may affect up to 1 in 100 people) condition called "Capillary Leak Syndrome" which causes blood to leak from the small blood vessels into your body and needs urgent medical attention.
- You have kidney injury (glomerulonephritis). Kidney injury has been seen in patients who received Granocyte. Call your doctor right away if you experience puffiness in your face or ankles, blood in your urine or brown-coloured urine or notice you urinate less than usual.

Tell a doctor or pharmacist as soon as possible if you have any of the following side effects:

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

- Pains in your bones, muscles, joint, back and in legs and arms, a headache, fever, and/or feel sick (nausea). If it happens the pain can be controlled with normal painkillers.
- Temporary alterations in blood tests including those related to your liver function, which usually do not require any additional precautions and normalize after the drug is stopped.
- After the donation of the blood stem cell you may feel tired. It is because of the fall in your red blood cells. Your white blood cell count may become high for a short period of time. You may also have a decrease in platelets count which could make you bleed or bruise more easily than normal.

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

- A reaction at the site of the injection.
- General aches and pains including abdominal pain

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

- Coughing up blood (haemoptysis).

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

- Bleeding from the lung (pulmonary haemorrhage).
- Inflammation of the aorta (the large blood vessel which transports blood from the heart to the body), see section 2.

Very rare side effects (may affect up to 1 in 10, 000 people):

• Skin problems like plum coloured, raised areas on your arms or legs and sometimes your face or neck with fever (signs of 'Sweet's syndrome'). There may also be raised red lumps with fever and headache (signs of 'Lyell's syndrome'). Also, other skin problems like red raised bruises on the legs or ulcers on your body with fever and joint pain.

• An allergic reaction. The signs include a rash, swallowing and breathing problems, swelling of your lips, face, throat or tongue.

Not known (frequency cannot be estimated from the available data):

▪ Blood test results indicating inflammation (e.g. C - reactive protein increased).

▪ Blood clots formation in veins and arteries.

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 (see details below).

UK - Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard.

Ireland - HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Granocyte

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

Do not use any of the parts of the Granocyte powder and solvent for solution kit after the expiry (EXP) date. The expiry date for Granocyte powder is given on the outer carton box, on the paper foil of the blister and on the label of each vial of Granocyte. The expiry date for the solvent (water for injection) is given on the label of the water pre-filled syringe.

The expiry date refers to the last day of that month.

Do not store above 30°C. Do not freeze.

After reconstitution or dilution immediate use is recommended. If needed, you may store the reconstituted or diluted solution up to 24 hours at 2°C -8°C (in a refrigerator).

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 protect the environment.

6. Contents of the pack and other information

What Granocyte contains

• The active substance is lenograstim (rHuG-CSF) 13.4 million International Units (equivalent to 105 micrograms) per mL after reconstitution.

• The active substance is lenograstim (rHuG-CSF) 33.6 million International Units (equivalent to 263 micrograms) per mL after reconstitution.

• The other ingredients in the powder are arginine, phenylalanine, methionine, mannitol (E421), polysorbate 20 and diluted hydrochloric acid.

Excipients known to have a recognised action or effect: phenylalanine

• The solvent used to reconstitute the solution is Water for Injections

What Granocyte looks like and contents of the packs
Granocyte is presented as [powder and a solvent for solution for injection/infusion in a pre-filled syringe].

Powder in a vial + 1mL of solvent in a pre-filled syringe with two needles (the larger cream coloured one for reconstitution (19G) and the smaller brown coloured one for administration (26G))

Granocyte is presented as [powder and a solvent for solution for injection/infusion].
Powder in a vial + 1mL of solvent in ampoule (UK market only)

GRANOCYTE is available in pack sizes of 1 or 5.

Not all pack sizes may be marketed

Marketing Authorisation Holder
UK
Chugai Pharma UK Ltd,
Mulliner House, Flanders Road,
Turnham Green, London
W4 1NN.

Ireland
Chugai Pharma France SAS
Tour Pacific
11-13 cours Valmy
92800 Puteaux
France

Manufacturer
SANOFI WINTHROP INDUSTRIE, Usine de Maisons-Alfort, 180 rue Jean-Jaurès, BP40
94702 Maisons-Alfort - Cedex -France

This medicinal product is authorised in the Member States of the EEA under the following names:
All Member States of the EEA: GRANOCYTE
Italy: GRANOCYTE and MYELOSTIM
For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:
UK and Ireland - Chugai Pharma UK Ltd, Mulliner House, Flanders Road, Turnham Green, London W4 1NN.

This leaflet was last revised in September 2022.
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The following information is intended for medical or healthcare professionals only:

Practical information on preparation and handling of the medicinal product for medical or healthcare professionals

Granocyte vials are for single-dose use only.

In view of the possible risk of microbial contamination, pre-filled syringe with solvent are for single use only.

Granocyte is for sub-cutaneous or intravenous use.

Preparation of the reconstituted solution

Aseptically add the extractable contents of one pre-filled syringe to the Granocyte vial using the 19G needle.

- Agitate gently until completely dissolved.
- Do not shake vigorously.
- The reconstituted parenteral solution appears transparent and free of particles.

Withdraw the required volume of the reconstituted solution from the vial, using the 19G needle.

- Administer immediately by sub-cutaneous injection using the 26G needle.

In case of intravenous use Granocyte has to be diluted after reconstitution.

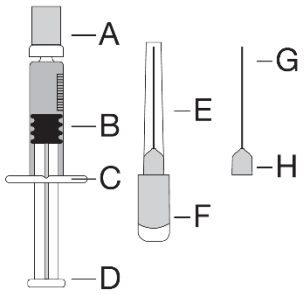
Granocyte is compatible with the commonly used administration sets for injection when diluted:

- in a 0.9% saline solution (polyvinyl chloride bags and glass bottles)
- or in a 5% dextrose solution (glass bottles)

Dilution of GRANOCYTE 13 million IU/mL to a final concentration of less than 0.26 million International Units/mL (2 µg/mL) is not recommended. 1 vial of reconstituted GRANOCYTE 13 million IU/mL should not be diluted in more than 50 mL under any circumstances

Dilution of GRANOCYTE 34 million IU/mL to a final concentration of less than 0.32 million International Units/mL (2.5 µg/mL) is not recommended. 1 vial of reconstituted GRANOCYTE 34 million IU/mL should not be diluted in more than 100 mL under any circumstances.

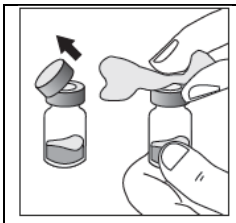
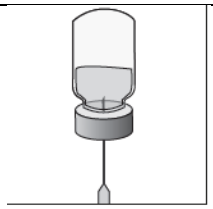
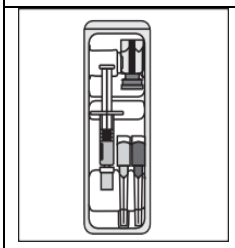
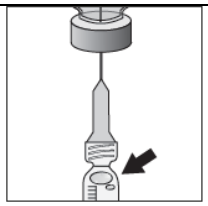
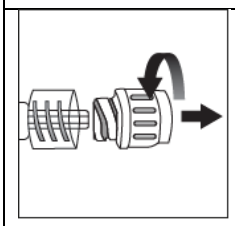
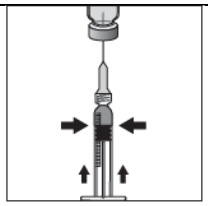
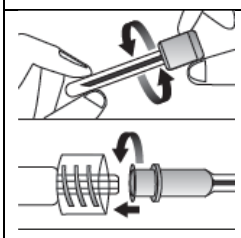
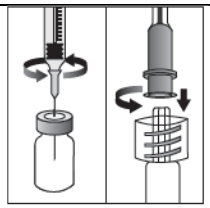
Any unused product/solution or waste material should be disposed of in accordance with local requirements

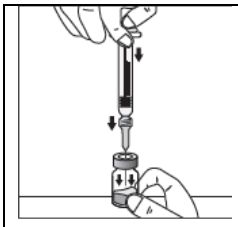
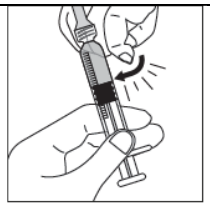
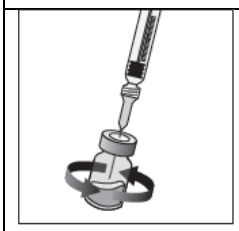
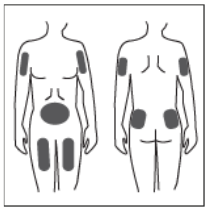


A: Tip-cap (including inner rubber insert)
B: Stopper
C: Backstop (must not be removed)
D: Plunger

Needles are protected in hard individual packaging made up of:
E: Needle sheath
F: Coloured cap (cream coloured or brown coloured)

G: Needle tip
H: Needle hub

	**Diagram 1** Remove the vial from the blister and remove the plastic cap from the vial. Clean the rubber stopper of the vial with a sterile alcohol wipe.		**Diagram 7** Keeping the needle and the syringe attached to the vial, turn the vial upside down. Partially withdraw the needle making sure the tip is in the solution. Hold the needle hub and syringe, pull back the plunger slowly to draw up as much as possible all the solution into the syringe.
	**Diagram 2** Remove the pre-filled syringe and the two needles (one with the cream coloured cap (19G) and one with the brown coloured cap (26G)) from the blister.		**Diagram 8** Check the syringe for air bubbles. If bubbles are in the syringe, hold the syringe straight up and tap the side of the syringe until bubbles float at the top. Push the bubbles out with the plunger.
	**Diagram 3** Unscrew the tip-cap from the syringe and remove it.		**Diagram 9** Push the plunger until the top of the stopper lines up with the next larger volume mark than what you need (in 0.1ml increments). For example, if you need 0,8 ml then push the plunger to the 0,9 ml mark
	**Diagram 4** Firmly grip the cream coloured needle packaging at both ends. Twist the cream coloured cap (clockwise or anti-clockwise) and pull it off. Holding the needle sheath, screw the needle hub onto the syringe.		**Diagram 10** Turn the vial upright and push the needle fully into the vial. Hold the needle hub, unscrew the syringe leaving the needle in the vial. Firmly grip the brown coloured needle packaging at both ends. Twist the brown coloured cap (clockwise or anti-clockwise) and pull it off. Holding the needle sheath, screw the needle hub onto the syringe. Remove the needle sheath.

	**Diagram 5** Remove the needle sheath. Keeping the vial on a flat surface, push the needle through the rubber stopper and then slowly push the plunger rod to inject the solvent into the vial.		**Diagram 11** Check the syringe for air bubbles. If bubbles are in the syringe, hold the syringe straight up and tap the side of the syringe until the bubbles float to the top. Push the bubbles out with the plunger. If necessary, adjust the volume to be administered.
	**Diagram 6** Swirl gently until the powder is completely dissolved. Do not shake vigorously.	 Front Back	GRANOCYTE is now ready for administration. Administer immediately by subcutaneous injection. **Location of the injection sites for subcutaneous administration.**