PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Pegfilgrastim Kamada

Solution for injection in a pre-filled syringe
6 mg/0.6 ml (10 mg/1 ml)
For subcutaneous administration

COMPOSITION:
Each pre-filled syringe contains:
pegfilgrastim 6 mg/0.6 ml

Inactive ingredients and allergenic in the product see section 2 "Important information about some of the ingredients of the medicine" and section 6 - "Further Information".

- **Read all of this leaflet carefully in its entirety before using this medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or to a pharmacist.
- Keep this leaflet. You may need to read it again.
- This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them, even if it seems to you that their symptoms of illness are similar.
- 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 – "Side effects".

Important information for your attention

- If you have been told that you are sensitive to certain types of sugars, consult the doctor before using Pegfilgrastim Kamada.
- Pegfilgrastim Kamada can be self-injected in your home after receiving instruction from a healthcare professional. Please carefully read the instructions for self-injection at the end of this leaflet.
- Following the doctor's instructions (dosage, times of injection, and duration of treatment) increases the chances for success of the treatment. In any case, do not discontinue the treatment without consulting the attending doctor. Please read sections 2 and 4 for broader safety information.
- Keep Pegfilgrastim Kamada in the refrigerator (see section 5 - "How should the medicine be stored?").
- The medicine, Pegfilgrastim Kamada pre-filled syringe, is intended for single-use!

Pegfilgrastim Kamada is a biosimilar product. For more information regarding biosimilar products please refer to the Ministry of Health website: https://www.gov.il/he/Departments/General/biosimilar
Any replacement or change in the dosage of a medicine containing Pegfilgrastim (the active ingredient in the medicine) must be carried out exclusively by the treating specialist doctor.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine Pegfilgrastim Kamada is used to reduce the duration of neutropenia (low white blood cell count) and the occurrence of febrile neutropenia (low white blood cell count with a fever), which can be caused by the use of cytotoxic chemotherapy (medicines that destroy rapidly growing cells), given at intervals of 14 days or more, for malignancy (with the exception of chronic myeloid leukemia [CML] and myelodysplastic syndromes [MDS]).

White blood cells are important as they help your body fight infection. These cells are very sensitive to the effects of chemotherapy, which can cause the number of these cells in your body to decrease. If white blood cells count falls below a certain level, the ability of your body to fight against the bacteria is damaged and you may have an increased risk of infection.

The doctor has given you Pegfilgrastim Kamada to encourage your bone marrow (part of the bone which makes blood cells) to produce more white blood cells that help your body fight infection.

Therapeutic group:
immunostimulants, colony stimulating factors.
Pegfilgrastim Kamada is a medicine from the group of proteins called granulocyte-colony stimulating factor (G-CSF).
Pegfilgrastim Kamada contains the active substance pegfilgrastim. Pegfilgrastim is a protein produced by biotechnology in bacteria called *E. coli*. It belongs to a group of proteins called cytokines and is very similar to a natural protein (granulocyte-colony stimulating factor = G-CSF) produced by your own body.

2. BEFORE USING THE MEDICINE

Do not use this medicine if:

you are sensitive (allergic) to the active ingredient pegfilgrastim, filgrastim, *E. coli* derived proteins, or any of the other ingredients which this medicine contains (listed in section 6 - "Further Information").

Special warnings regarding use of the medicine
Before using Pegfilgrastim Kamada tell the doctor:

- If you experience an allergic reaction including weakness, drop in blood pressure, difficulty breathing, swelling of the face (anaphylaxis), redness and flushing, skin rash and areas of the skin that itch.
- If you experience a cough, fever and difficulty breathing. This can be a sign of Acute Respiratory Distress Syndrome (ARDS).
- 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 could be symptoms of a condition called "Capillary Leak Syndrome", which causes blood to leak from the small blood vessels into your body. See section 4 – "Side effects".
- If you get left upper abdominal pain or pain at the tip of your shoulder. This may be a sign of a problem with your spleen (splenomegaly).
- If you have recently had a serious lung infection (pneumonia), fluid in the lungs (pulmonary edema), inflammation of the lungs (interstitial lung disease) or an abnormal chest X-ray (lung infiltration).
- If you are aware of any altered blood cell counts (e.g., increase in white blood cells or anemia) or decreased blood platelet counts, which reduces the ability of your blood to clot (thrombocytopenia). Your doctor may want to monitor you more closely.
- If you have sickle-cell anemia. Your doctor may monitor your condition more closely.
- if you are a patient with breast cancer or lung cancer, Pegfilgrastim Kamada in combination with chemotherapy and/or radiation therapy may increase your risk of a precancerous blood condition called myelodysplastic syndrome (MDS) or a blood cancer called acute myeloid leukemia (AML). Symptoms may include tiredness, fever, and easy bruising or bleeding.
- 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 these could be signs of a severe allergic reaction.
- If you have symptoms of inflammation of aorta (the large blood vessel which transports blood from the heart to the body), this 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.

Your doctor will check your blood and urine regularly as Pegfilgrastim Kamada can harm the tiny filters inside your kidneys (glomerulonephritis).

Severe skin reactions (Stevens-Johnson syndrome) have been reported with the use of Pegfilgrastim Kamada. Stop using Pegfilgrastim Kamada and seek medical attention immediately if you notice any of the symptoms described in section 4 - "Side effects".

You should talk to your doctor about your risks of developing cancers of the blood. If you develop or are likely to develop cancers of the blood, you should not use Pegfilgrastim Kamada, unless instructed by your doctor.

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

Children and adolescent
There is no information regarding the safety and efficacy of Pegfilgrastim Kamada in children and adolescents.

Testing and monitoring
During the period of treatment with the product, the doctor will refer you regularly to blood and urine tests, since Pegfilgrastim Kamada may harm the kidneys (see extension above).

Interactions/Drug interactions
If you are taking or have recently taken, or might take any other medicines, including non-prescription medicines and nutritional supplements, tell your doctor or pharmacist.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicines.
Pregnancy
There is no information, or the information is limited regarding the use of pegfilgrastim in pregnancy.
Pegfilgrastim Kamada is not recommended for use during pregnancy or in women of childbearing age who do not use contraceptives. If you are pregnant, think you may be pregnant or plan to conceive, consult the doctor before using this medicine. Please inform the doctor if you become pregnant during the treatment with Pegfilgrastim Kamada.
Breast-feeding
There is insufficient information on the excretion of the drug in breast milk, a risk to newborns/infants cannot be ruled out. You must stop breast-feeding if you are using Pegfilgrastim Kamada, unless the doctor instructs you otherwise.

Driving and using machines
Pegfilgrastim Kamada has no or negligible effect on the ability to drive or use machines.

Important information about some of the ingredients of the medicine
Pegfilgrastim Kamada contains sorbitol and sodium.
This medicine contains 30 mg sorbitol in each pre-filled syringe which is equivalent to 50 mg/mL.
This medicinal product contains less than 1 mmol sodium (23 mg) per 6 mg dose, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

The product should always be used according to the doctor's instructions. You should check with the doctor or pharmacist if you are unsure about the dosage and how to use the product.
The dosage and treatment regimen will be determined by the doctor only. The usual dose is:
one 6 mg subcutaneous injection (injection under your skin) using a pre-filled syringe and it should be given at least 24 hours after your last dose of chemotherapy at the end of each chemotherapy cycle.
Do not exceed the recommended dose.
Do not shake Pegfilgrastim Kamada vigorously as this may affect its activity.

Method of administration
Injecting the medicine Pegfilgrastim Kamada yourself
Your doctor may decide that it would be more convenient for you to inject Pegfilgrastim Kamada yourself. Your doctor or nurse will show you how to inject yourself. Do not try to inject yourself if you have not been trained.
For further instructions on how to inject yourself with Pegfilgrastim Kamada, please read the section at the end of this leaflet.

If you accidentally injected a higher dosage of the medicine Pegfilgrastim Kamada
If you use more Pegfilgrastim Kamada than you should, contact a doctor, pharmacist, or nurse.
If you used an overdose or if a child accidentally injected or swallowed the medicine, refer to the doctor immediately or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to inject the medicine Pegfilgrastim Kamada
If you are injecting yourself and have forgotten a dose of Pegfilgrastim Kamada, you should contact the doctor to discuss when you should inject the next dose. You must persist in the treatment recommended by the doctor.

How can you contribute to the success of the treatment?
Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have any further questions on the use of the medicine, consult a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicine, use of this medicine may cause side effects in some users. Do not be alarmed when reading the list of side effects; you may not experience any of them.

Please tell the doctor immediately if you have any of the following or a 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 patients) condition called "Capillary Leak Syndrome", which causes blood to leak from the small blood vessels into your body and needs urgent medical attention.

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

- Bone pain. The doctor will tell you what you can take to ease the bone pain.
- Nausea and headaches.

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

- Pain at the site of injection.
- General aches and pains in the joints and muscles.
- Some changes may occur in your blood, but these will be detected by routine blood tests. Your white blood cell count may become high for a short period of time. Your platelet count may become low which might result in bruising.

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

- Allergic-type reactions including redness and flushing, skin rash, and raised areas of the skin that itch.
- Serious allergic reactions including anaphylaxis (weakness, drop in blood pressure, difficulty breathing, swelling of the face).
- Increased spleen size.
- Spleen rupture. Some cases of splenic rupture were fatal. It is important that you contact the doctor immediately if you experience pain in the upper left side of the abdomen or left shoulder pain since this may relate to a problem with your spleen.
- Breathing problems. If you have a cough, fever and difficulty breathing, please tell the doctor.
- Sweet's syndrome (plum-colored, raised and painful lesions on the limbs and sometimes the face and neck with fever) has occurred, but other factors may play a role.
- Cutaneous vasculitis (inflammation of the blood vessels in the skin).
- Damage to the tiny filters inside your kidneys (glomerulonephritis).
- Redness at the site of injection.
- Coughing up blood (hemoptysis).
- Blood disorders (myelodysplastic syndrome [MDS] or acute myeloid leukemia [AML]).

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

- Inflammation of aorta (the large blood vessel which transports blood from the heart to the body), see section 2 – "Before using the medicine".
- Bleeding from the lung (pulmonary hemorrhage).
- Stevens-Johnson syndrome, which can appear as reddish target-like or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu -like symptoms. Stop using Pegfilgrastim Kamada if you develop these symptoms and contact the doctor or seek medical attention immediately. See also section 2 – "Before using the medicine".

If a side effect occurs, if one of the side effects worsens, or if you experience a side effect not mentioned in the leaflet, you must consult your doctor.

Reporting of side effects:
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il
In addition, you can report to Kamada Ltd. by email: pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and all other medicines, must be stored in a safe place out of the reach and sight of children and/or infants, to avoid poisoning.
Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date which appears on the carton and the syringe label. The expiry date refers to the last day of that month.
Store in a refrigerator (2°C–8°C).

Pegfilgrastim Kamada can be taken out of the refrigerator and kept at room temperature (not exceeding 30°C) for no longer than 3 days. Once a syringe has been removed from the refrigerator and has reached room temperature (did not exceed 30°C) it must either be used within 3 days or disposed of.

Do not freeze. Pegfilgrastim Kamada may be used if it is accidentally frozen for a single period of less than 24 hours.
Keep the medicine in the outer carton in order to protect from light.

Do not use this medicine if you notice it is cloudy or there are particles in it.

The medicine, Pegfilgrastim Kamada pre-filled syringe, is intended for single-use only!

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

6. FURTHER INFORMATION

In addition to the active substance, the medicine also contains:
d-Sorbitol (E-420), glacial Acetic Acid, sodium hydroxide, polysorbate 20, water for injection.
The medicine Pegfilgrastim Kamada is essentially "sodium-free".

How does the medicine look and what are the contents of the package:
The medicine Pegfilgrastim Kamada is a solution for injection in a pre-filled syringe (6 mg/0.6 ml).

Each package contains 1 pre-filled glass syringe with an attached stainless-steel needle cap. The syringes are provided with an automatic needle safety guard.
The solution is clear and colorless.

The registration holder and address: Kamada Ltd., Beit Kama, MP Negev 8532500

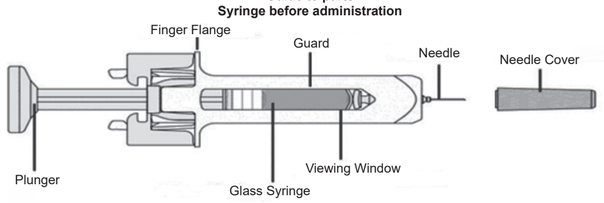
Manufacturer's name and address: USV Private Limited, H-13, 16, 16-A, 17, 18, 19, 20, 21 and E-22, O.I.D.C., Mahatma Gandhi Udyog Nagar, Dabhel, Daman, 396 210, India

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 173-91-37554

Revised in March 2024.

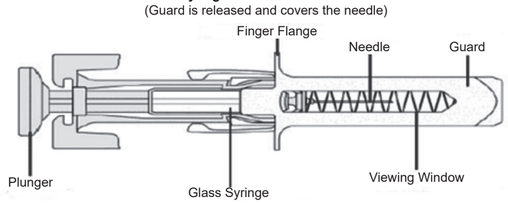
7. INSTRUCTIONS FOR INJECTING WITH THE PEGFILGRASTIM KAMADA PRE-FILLED SYRINGE

Guide to parts
Syringe before administration



Caution: *Avoid contact with the plunger and needle during the preparation of the syringe, The safety device is normally activated by pressure from the plunger on the syringe.*

Syringe after administration
(Guard is released and covers the needle)



Important
Before you use a Pegfilgrastim Kamada pre-filled syringe with automatic needle guard, read this important information:

- It is important that you do not try to give yourself the injection unless you have received training from the doctor, nurse or pharmacist.
- The medicine Pegfilgrastim Kamada is given as an injection into the tissue right under the skin (subcutaneous use).

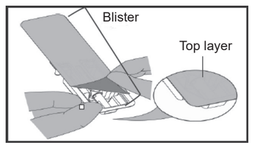
X **Do not** remove the grey needle cap from the pre-filled syringe until you are ready to inject.
X **Do not** use the pre-filled syringe if it has been dropped on a hard surface. Use a new pre-filled syringe and contact your doctor or healthcare provider.
X **Do not** attempt to activate the pre-filled syringe prior to injection.
X **Do not** attempt to remove the clear pre-filled syringe safety guard from the pre-filled syringe.
X **Do not** attempt to remove the peelable label on the pre-filled syringe barrel before administering your injection.
Contact your doctor or healthcare provider if you have any questions.

Step 1: Prepare

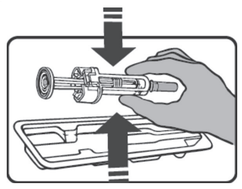
A. Remove the pre-filled syringe tray from the package and gather the supplies needed for your injection: alcohol wipes, a cotton ball or gauze pad, a plaster and a sharps disposal container (not included).
For a more comfortable injection, leave the pre-filled syringe at room temperature for about 30 minutes before injecting. Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the new pre-filled syringe and the other supplies.
X **Do not** try to warm the syringe by using a heat source such as hot water or microwave.
X **Do not** leave the pre-filled syringe exposed to direct sunlight.
X **Do not** shake the pre-filled syringe.
Keep pre-filled syringe out of the sight and reach of children.

B. Warning/Precaution: ensure there is no loose fragment or fluid inside the pack. In case of doubt **DO NOT** open this pack and take another pack instead.
Open the blister by peeling back the top layer all the way off the blister as shown.



C. Warning/Precaution: **DO NOT** lift the product by holding the plunger or needle cover.
Remove the pre-filled syringe from blister as shown.



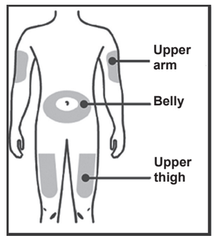
D. Inspect the medicine content through the viewing window of the pre-filled syringe.
X **Do not** use the pre-filled syringe if:

- The medicine is cloudy or there are particles in it. The liquid must be clear and colourless.
- Any part appears cracked or broken.
- The grey needle cap is missing or not securely attached.
- The expiry date printed on the label has passed the last day of the month shown.

In all cases, contact your doctor or healthcare provider.

Step 2: Get ready

A. Wash your hands thoroughly. Prepare and clean your injection site.

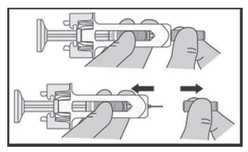


You can use:

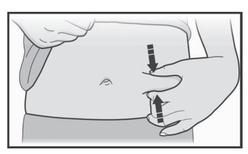
- Upper part of your thigh.
- Belly, except for a 5 cm area right around your belly button.
- Outer area of upper arm (only if someone else is giving you the injection).

Clean the injection site with an alcohol wipe. Let your skin dry.
X **Do not** touch the injection site before injecting.
! **Do not** inject into areas where the skin is tender, bruised, red or hard. Avoid injecting into areas with scars or stretch marks.

B. Warning/Precaution: DO NOT twist the needle cover or touch the needle or plunger.
Pull the needle cover straight off as shown and handle the guard to avoid injuries or bending the needle.



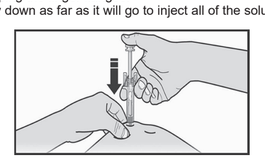
C. Pinch your injection site to create a firm surface.



! It is important to keep the skin pinched when injecting.

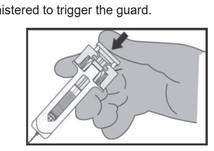
Step 3: Inject

A. INSERT the needle into skin.
Push the plunger while grasping the finger flanges.
Push the plunger all the way down as far as it will go to inject all of the solution.



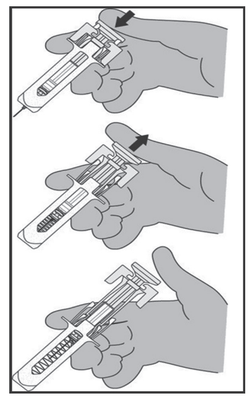
X **Do not** touch the injection site before injecting.

B. The entire dose has to be administered to trigger the guard.



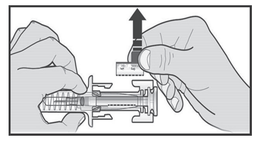
C. After the injection is complete, one of the below alternatives can be followed:

- Remove the needle from the injection site and release the plunger until the entire needle is covered by the guard.
- Release the plunger until the needle is covered and then remove the syringe from the injection site.



! Warning/Precaution: If the guard is not activated or only partially activated, discard the syringe without replacing the needle cover.

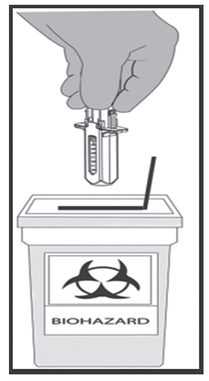
Healthcare professionals only
The trade name of the medicine should be clearly recorded in the patient file.



Turn the plunger to move the label into a position where you can remove the syringe label.

Step 4: Finish

A. Dispose of the used medicine immediately in a Sharps container or as instructed by your healthcare provider.



Medicines should be disposed of in accordance with local requirements. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment. Keep the syringe and sharps disposal container out of sight and reach of children.
X **Do not** reuse the syringe.
X **Do not** recycle syringes or throw them away via household waste.

B. Examine the injection site.
If there is blood, press a cotton ball or gauze pad on your injection site. **Do not** rub the injection site. Apply a plaster if needed.