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

The medicine is dispensed with a doctor's prescription only

PEGIL

Solution for Injection in Pre-filled Syringe

6 mg/0.6 mL

For subcutaneous administration

Composition:

Each pre-filled syringe contains:

Pegfilgrastim 6 mg/0.6 ml

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

- **Read the leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor, pharmacist or nurse.
- Keep this leaflet. You may need to read it again.
- This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.
- If any side effects occur, consult a 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 **Pegil**.
- **Pegil** can be self-injected in your home after receiving instruction from a healthcare professional. Please carefully read the instructions for self-injection appearing in the Instructions for Use Leaflet attached to the package.
- Carefully following the doctor's instructions (dosage, times of injection and duration of treatment) increases the chances for treatment success. In any case, do not discontinue the treatment without consulting the attending doctor. Please read sections 2 and 4 for extensive safety information.
- Keep **Pegil** in the refrigerator (see section 5 – "How Should The Medicine Be Stored?").
- The medicine, **Pegil** pre-filled syringe, is intended for single use!

Note that it is important that you verify, each time you receive the medicine in the pharmacy, that you receive the medicine prescribed for you by the attending specialist physician. If the medicine you received looks different than the one you usually receive, or if the instructions for use have changed, please refer to the pharmacist immediately and confirm that you received the correct medicine. Every switch or dosage change of a medicine containing pegfilgrastim (the active ingredient in the medicine) must only be made by the attending specialist physician. Please check that the trade name of the preparation prescribed for you by the specialist physician is identical to the name of the medicine you received from the pharmacist.

1. WHAT IS THE MEDICINE INTENDED FOR?

Pegil contains the active ingredient pegfilgrastim. Pegfilgrastim is a protein produced by biotechnological methods in bacteria called *E. coli*. The protein 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 body.

Pegil is used to reduce the duration of neutropenia (low white blood cell count) and to reduce the risk of febrile neutropenia occurrence (low white blood cell count with a fever), which can be caused by cytotoxic chemotherapy (medicines that destroy rapidly growing cells). 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 cell counts fall below a certain level, the ability of your body to defend itself against bacteria becomes impaired and you may be at increased risk of infection.

Your doctor has given you **Pegil** 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

Pegil is a medicine from the group of proteins called granulocyte-colony stimulating factor (G-CSF).

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

You are sensitive (allergic) to pegfilgrastim, filgrastim, *E. coli*-derived proteins, or to any of the additional ingredients contained in the medicine (listed in section 6 – "Further Information").

Special warnings regarding use of this medicine

Before treatment with **Pegil**, tell your doctor, pharmacist or nurse:

- 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 ARDS (Acute Respiratory Distress Syndrome).
- If you have one 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 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 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.
- 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 those symptoms.

Your doctor will check your blood and urine regularly as **Pegil** may harm the small filters inside your kidneys (glomerulonephritis).

Severe skin reactions (Stevens-Johnson syndrome) have been reported with the use of pegfilgrastim. Stop using **Pegil** 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, do not use **Pegil**, unless instructed to do so by your doctor.

Loss of response to pegfilgrastim

If you no longer respond, or fail to maintain a response to pegfilgrastim treatment, your doctor will investigate the reasons why, including whether you have developed antibodies which neutralize pegfilgrastim's activity.

Drug interactions

If you are taking, have recently taken, or may take, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Pregnancy and breastfeeding

Consult your doctor or pharmacist before taking any medicines.

Pegil has not been tested in pregnant women.

If you are pregnant, think you may be pregnant, or are planning to become pregnant, consult your doctor before using this medicine.

Stop breastfeeding if you are using **Pegil**, unless the doctor directs you otherwise.

Driving and using machinery

Pegil has no effect, or its effect is negligible, on the ability to drive or use machinery.

Important information about some of the ingredients of the medicine

Pegil contains 30 mg sorbitol (a type of sugar) in each pre-filled syringe, which is equivalent to 50 mg/ml.

This medicine contains less than 1 mmol (23 mg) sodium per 6 mg dose, that is to say, the medicine is essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Pegil is intended for use in adults aged 18 and over.

Always use the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and the 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 shake **Pegil** vigorously as it may impair its activity.

Do not exceed the recommended dose.

Self-injection of Pegil

Your doctor may decide that it would be more convenient for you to inject **Pegil** 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 **Pegil**, please read the Instructions for Use Leaflet, attached to the package.

If you accidentally injected a higher dosage of Pegil

If you used more **Pegil** than required, refer to your doctor, pharmacist or nurse.

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to inject Pegil

If you inject the medicine yourself and you forgot a dose of **Pegil**, refer to your doctor to consult when you should inject the next dose.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of this medicine, ask your doctor, pharmacist or nurse.

4. SIDE EFFECTS

As with any medicine, use of **Pegil** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Please tell your doctor immediately if you have one 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 (an effect that occurs in 1-10 in 1,000 users) condition called "Capillary Leak Syndrome", which causes blood to leak from the small blood vessels into your body and requires urgent medical treatment.

Very common side effects (effects that occur in more than one user in ten):

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

Common side effects (effects that occur in 1-10 in 100 users):

- 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 (effects that occur in 1-10 in 1,000 users):

- 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).
- Spleen enlargement.
- Spleen rupture. Some cases of splenic rupture were fatal. It is important that you contact your 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 your doctor.
- Cases of Sweet's syndrome (purplish, painful and raised lesions on the limbs and sometimes on the face and neck, accompanied by fever) have occurred, but other factors may be involved.
- Cutaneous vasculitis (inflammation of the blood vessels in the skin).
- Damage to the small filters inside your kidneys (glomerulonephritis).
- Redness at the site of injection.
- Coughing up blood (hemoptysis).

Rare side effects (effects that occur in 1-10 in 1,000 users):

- Inflammation of the 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, as skin peeling, ulcers of mouth, throat, nose, genitals and eyes; can be preceded by fever and flu-like symptoms. Stop using **Pegil** if you develop these symptoms and contact your 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 suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Reporting 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, they can be reported to "Unipharm Ltd." at: https://unipharm.co.il/

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning.

Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (Exp. date) that appears on the carton package and on the syringe label. The expiry date refers to the last day of that month.

Storage conditions:

Store in a refrigerator (2°C-8°C) in the outer carton package, in order to protect from light.

Pegil can be taken out of the refrigerator and stored at room temperature for up to 72 hours. Dispose of syringes that have been stored at room temperature for over 72 hours.

Do not freeze. If frozen, defrost in the refrigerator before use. Dispose of a syringe that has been frozen more than once.

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

Pegil pre-filled syringe is intended for single use only!

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

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

D-sorbitol, Acetate, Polysorbate 20, Sodium, Water for injection.

See section 2 – "Important information about some of the ingredients of the medicine".

What the medicine looks and the contents of the package

Pegil is a solution for injection in a pre-filled syringe (6 mg/0.6 ml).

Each package contains one pre-filled syringe, which includes a needle for injection and needle cover. The syringe is packaged in a tray (blister). The syringe is provided with an automatic needle guard.

The solution is clear and colorless.

License holder and importer: Unipharm Trading Ltd., P.O.B. 21429 Tel Aviv, 6121301.

Revised in November 2020.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

165 36 35770 00

1220B

unipharm ltd. KR/DRUGS/KTK/28D/07/2006

INSTRUCTIONS FOR USE

PEGIL

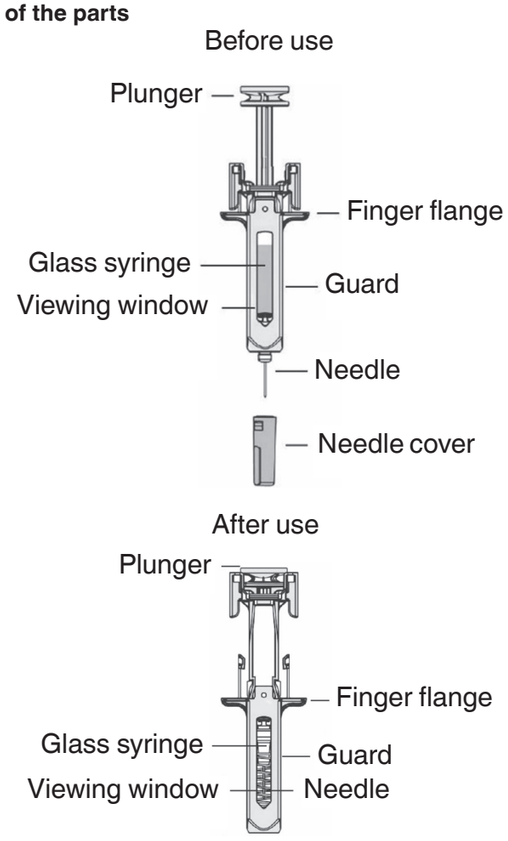
Solution for Injection in Pre-filled Syringe

6 mg/0.6 mL

For subcutaneous administration

INSTRUCTIONS FOR USE OF THE PEGIL PRE-FILLED SYRINGE:

Description of the parts



Important

Before using Pegil 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 your doctor or another medical authority.
- **Pegil** is given as an injection into the tissue just under the skin (subcutaneous injection).

X **Do not** remove the gray needle cover 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 call the doctor or another medical authority.
X **Do not** attempt to activate the pre-filled syringe prior to injection.
X **Do not** attempt to remove the clear syringe safety guard from the pre-filled syringe.
X **Do not** attempt to remove the peelable label from the pre-filled syringe barrel before administering your injection.

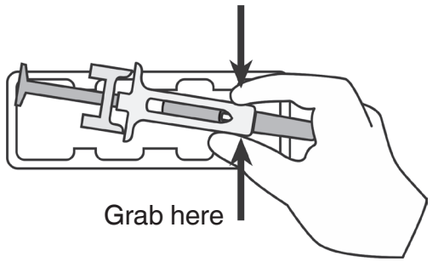
Contact your doctor or another medical authority if you have further questions.

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).

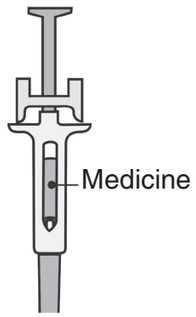
For a more comfortable injection, leave the pre-filled syringe at room temperature for about 30 minutes before injecting. Wash your hands thoroughly with soap and water.
Place the new pre-filled syringe and the other supplies on a clean, well-lit work surface.
X **Do not** try to warm the syringe by using a heat source such as hot water or a microwave.
X **Do not** leave the pre-filled syringe exposed to direct sunlight.
X **Do not** shake the pre-filled syringe.
- **Keep pre-filled syringes out of the reach and sight of children.**

B. Open the tray by peeling away the cover. Grab the pre-filled syringe safety guard to remove the pre-filled syringe from the tray.



For safety reasons:
X **Do not** grasp the plunger.
X **Do not** grasp the gray needle cover.

C. Inspect the medicine and the pre-filled syringe.

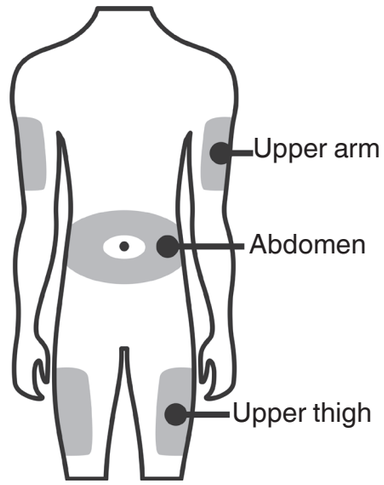


X **Do not** use the pre-filled syringe if:
- The medicine is cloudy or there are particles in it. The liquid must be clear and colorless.
- Any part appears cracked or broken.
- The gray needle cover is missing or not securely attached.
- The expiry date which is stated on the label has passed the last day of the month shown.

In all cases, contact your doctor or another medical authority.

Step 2: Get ready

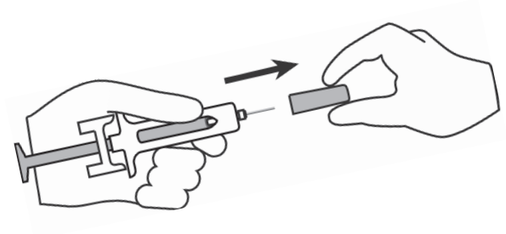
A. Wash your hands thoroughly. Prepare and clean your injection site.



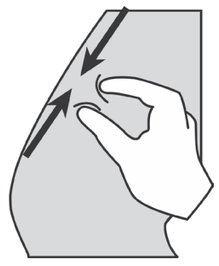
Areas appropriate for injection:
- The upper part of your thigh.
- The abdomen, except for the 5 cm area right around the belly button.
- The outer area of upper arm (only if someone else is giving you the injection).

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

B. Carefully pull the gray needle cover straight off and away from your body.



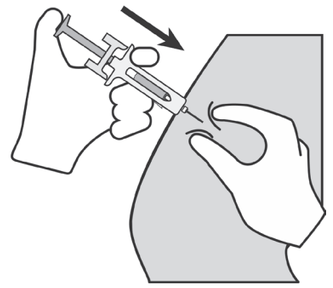
C. Pinch your injection site to create a firm surface.



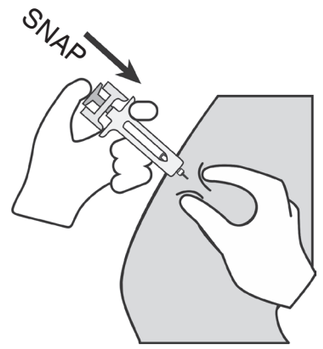
- It is important to keep pinching the skin when injecting.

Step 3: Inject

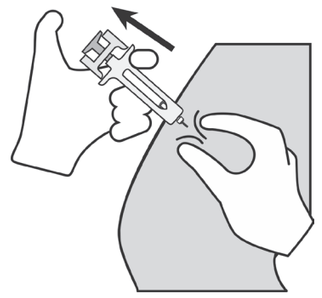
A. Hold the pinch. **Insert** the needle into the skin.



Do not touch the cleaned injection area of the skin.
B. **Push** the plunger with slow and constant pressure until you feel or hear a snapping sound. Push the plunger all the way down as far as it will go until you hear the snap.



It is important to push the plunger down until you hear the snap, to release the full dose.
C. **Release** your thumb. Then **lift** the syringe off the skin.



After releasing the plunger, the syringe safety guard will safely cover the injection needle.
X **Do not** put the gray needle cover back on used syringes.

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

Step 4: Finish

A. Discard the used pre-filled syringe and other supplies in a sharps disposal container.

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

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

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