GRANIX® (tbo-filgrastim) injection, for subcutaneous use

Full Prescribing Information:

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GRANIX safely and effectively. See full prescribing information for GRANIX.

GRANIX® (tbo-filgrastim) injection, for subcutaneous use

Initial U.S. Approval: 2012

--- RECENT MAJOR CHANGES ---

Contraindications (4) 02/2017
Warnings and Precautions, Glomerulonephritis (5.5) 02/2017

--- INDICATIONS AND USAGE ---

GRANIX (tbo-filgrastim) is a leukocyte growth factor indicated for reduction in the duration of severe neutropenia in patients with non-myoeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. (1)

DOSAGE AND ADMINISTRATION:

- Recommended dose: 5 mcg/kg per day administered as a subcutaneous injection.
- Administer the first dose no earlier than 24 hours following myelosuppressive chemotherapy. Do not administer within 24 hours prior to chemotherapy (2.1)

DOSAGE FORMS AND STRENGTHS:

- Injection: 300 mcg/0.5 mL solution in single-dose prefilled syringe
- Injection: 480 mcg/0.8 mL solution in single-dose prefilled syringe

CONTRAINDICATIONS:

Patients with a history of serious allergic reactions to filgrastim or pegfilgrastim products. (4)

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

GRANIX is indicated to reduce the duration of severe neutropenia in patients with non-myoeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

The recommended dose of GRANIX is 5 mcg/kg per day administered as a subcutaneous injection. Administer the first dose of GRANIX no earlier than 24 hours following myelosuppressive chemotherapy. Do not administer GRANIX within 24 hours prior to chemotherapy.

Daily dosing with GRANIX should continue until the expected neutrophil nadir is passed and the neutrophil count has recovered to the normal range. Monitor complete blood count (CBC) prior to chemotherapy and twice per week until recovery.

2.2 General Considerations for Administration

GRANIX may be administered by either a healthcare professional or by a patient or caregiver. Before a decision is made to allow GRANIX to be administered by a patient or caregiver, ensure that the patient is an appropriate candidate for self-administration or administration by a caregiver. Proper training on storage, preparation, and administration technique should be provided. If a patient or caregiver is not an appropriate candidate for any reason, then in such patients, GRANIX should be administered by a healthcare professional.

Dispense only the pre-filled syringe to properly administer an injection after training by a healthcare professional. Visually inspect parenteral drug products for particulate matter and discoloration prior to administration. Do not administer GRANIX if discoloration or particulates are observed.

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*Sections or subsections omitted from the full prescribing information are not listed.

The prefilled syringe is for single-dose only. Discard unused portions. GRANIX and all its components are not made with natural rubber latex. Recommended sites for subcutaneous GRANIX injections include the abdomen (except for the two-inch area around the navel), the front of the middle thighs, the upper outer areas of the buttocks, or the upper back portion of the upper arms. The injection site should be varied daily. GRANIX should not be injected into an area that is tender, red, bruised or hard, or that has scars or stretch marks.

2.3 Instructions for Use of the Safety Needle Guard Device by Healthcare Professionals

Hold the syringe assembly by the open sides of the device and remove the needle shield. Expel any extra volume depending on dose needed.

Inject GRANIX subcutaneously as recommended [see Dosage and Administration (2.2)].
GRANIX® (tbo-filograstim) injection

Push the plunger as far as it will go to inject all the medication. Injection of the entire prefilled syringe contents is necessary to activate the needle guard.

Slowly let go of the plunger and allow the empty syringe to move up inside the device until the entire needle is guarded.

With the plunger still pressed all the way down, remove the needle from the skin.

Discard the syringe assembly in approved containers.

3 DOSAGE FORMS AND STRENGTHS
Injection: 300 mcg/0.5 mL solution in single-dose prefilled syringe
Injection: 480 mcg/0.8 mL solution in single-dose prefilled syringe

4 CONTRAINDICATIONS
GRANIX is contraindicated in patients with a history of serious allergic reactions to filgrastim or pegfilgrastim products [see Warnings and Precautions (5.3)].

5 WARNINGS AND PRECAUTIONS
5.1 Splenic Rupture
Splenic rupture, including fatal cases, can occur following administration of filgrastim products. In patients who report upper abdominal or shoulder pain after receiving GRANIX, discontinue GRANIX and evaluate for an enlarged spleen or splenic rupture.

5.2 Acute Respiratory Distress Syndrome (ARDS)
Acute respiratory distress syndrome (ARDS) can occur in patients receiving filgrastim products. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving GRANIX, for ARDS. Discontinue GRANIX in patients with ARDS.

5.3 Allergic Reactions
Serious allergic reactions, including anaphylaxis, can occur in patients receiving GRANIX. Reactions can occur on initial exposure. The administration of antihistamines, steroids, bronchodilators, and/or epinephrine may reduce the severity of the reactions. Permanently discontinue GRANIX in patients with serious allergic reactions. Do not administer GRANIX to patients with a history of serious allergic reactions to filgrastim or pegfilgrastim.

5.4 Use in Patients with Sickle Cell Disease
Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving filgrastim products. Consider the potential risks and benefits prior to the administration of GRANIX in patients with sickle cell disease. Discontinue GRANIX in patients undergoing a sickle cell crisis.

5.5 Glomerulonephritis
Glomerulonephritis can occur in patients receiving filgrastim products. The diagnoses were based on azotemia, hematuria (microscopic and macroscopic), proteinuria, and renal biopsy. Generally, events of glomerulonephritis resolved after dose reduction or discontinuation of the filgrastim product. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of GRANIX.

5.6 Capillary Leak Syndrome
Capillary leak syndrome (CLS) can occur in patients receiving filgrastim products and is characterized by hypotension, hypoalbuminemia, edema and hemococoncentration. Episodes vary in frequency, severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care.

5.7 Potential for Tumor Growth Stimulatory Effects on Malignant Cells
The granulocyte colony-stimulating factor (G-CSF) receptor through which GRANIX acts has been found on tumor cell lines. The possibility that GRANIX acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which GRANIX is not approved, cannot be excluded.

6 ADVERSE REACTIONS
The following potential serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Spleenic Rupture [see Warnings and Precautions (5.1)]
- Acute Respiratory Distress Syndrome [see Warnings and Precautions (5.2)]
- Serious Allergic Reactions [see Warnings and Precautions (5.3)]
- Use in Patients with Sickle Cell Disease [see Warnings and Precautions (5.4)]
- Glomerulonephritis [see Warnings and Precautions (5.5)]
- Capillary Leak Syndrome [see Warnings and Precautions (5.6)]
- Potential for Tumor Growth Stimulatory Effects on Malignant Cells [see Warnings and Precautions (5.7)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

GRANIX clinical trials safety data are based upon the results of three randomized clinical trials in patients receiving myeloablative chemotherapy for breast cancer (N=348), lung cancer (N=240) and non-Hodgkin's lymphoma (N=92). In the breast cancer study, 96% of patients were female, the median age was 50 years, and 86% of patients were Caucasian. In the lung cancer study, 80% of patients were male, the median age was 58 years, and 95% of patients were Caucasian. In the non-Hodgkin's lymphoma study, 52% of patients were male, the median age was 55 years, and 88% of patients were Caucasian. In all three studies a placebo (Cycle 1 of the breast cancer study only) or a non-US-approved filgrastim product were used as controls. Both GRANIX and the non-US-approved filgrastim product were administered at 5 mcg/kg subcutaneously once daily beginning one day after chemotherapy for at least five days and continued to a maximum of 14 days or until an ANC of ≥10,000 x 10^6/L after nadir was reached.

Bone pain was the most frequent treatment-emergent adverse reaction that occurred in at least 1% or greater in patients treated with GRANIX at the recommended dose and was numerically two times more frequent than in the placebo group. The overall incidence of bone pain in Cycle 1 of treatment was 3.4% (3.4% GRANIX, 1.4% placebo, 7.5% non-US-approved filgrastim product).

Leukocytosis
In clinical studies, leukocytosis (WBC counts > 100,000 x 10^6/L) was observed in less than 1% patients with non-myeloid malignancies receiving GRANIX. No complications attributable to leukocytosis were reported in clinical studies.

Additional Adverse Reactions
Other adverse reactions known to occur following administration of filgrastim products include myalgia, headache, vomiting, cutaneous vasculitis and thrombocytopenia.

6.2 Immunogenicity
As with all therapeutic proteins, there is a potential for immunogenicity. The incidence of antibody development in patients receiving GRANIX has not been adequately determined.

6.3 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of GRANIX. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Sweet's syndrome (acute febrile neutrophilic dermatosis), asthma, diarrhea, and fatigue

7 DRUG INTERACTIONS
No formal drug interaction studies between GRANIX and other drugs have been performed. Drugs which may potentiate the release of neutrophils, such as lithium, should be used with caution.

Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone imaging changes. This should be considered when interpreting bone-imaging results.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
The limited published data on filgrastim product use during pregnancy are insufficient to inform a drug-associated risk. In animal reproduction studies, administration of tbo-filograstim to pregnant rabbits during organogenesis resulted in increased spontaneous abortion and fetal malformations at systemic exposures 50-90 times the human exposure expected at the recommended human dose (see Data). GRANIX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population(s) are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.
In an embryofetal developmental study, pregnant rabbits were administered subcutaneous doses of tbo-filgrastim during the period of organogenesis at 1, 10 and 100 mcg/kg/day. Increased abortions were evident in rabbits treated with tbo-filgrastim at 100 mcg/kg/day. This dose was maternally toxic as demonstrated by reduced body weight. Other embryofetal findings at this dose level consisted of placental weight loss, decrease in mean live litter size and fetal weight, and fetal malformations such as malformed hind limbs and cleft palate. The dose of 100 mcg/kg/day corresponds to a systemic exposure (AUC) of approximately 50-90 times the exposures observed in patients treated with the clinical tbo-filgrastim dose of 5 mcg/kg/day.

8.2 Lactation

No data are available regarding the presence of tbo-filgrastim in human milk, the effects of the drug on the breast fed infant, or the effects of the drug on milk production. Another filgrastim product was detected in human milk for up to 7 days after filgrastim administration.

8.4 Pediatric Use

Among 677 cancer patients enrolled in clinical trials of GRANIX, a total of 111 patients were 65 years of age and older. No overall differences in safety or effectiveness were observed between patients age 65 and older and younger patients.

10. OVERDOSE

No case of overdose has been reported.

11. DESCRIPTION

GRANIX (tbo-filgrastim) is a non-glycosylated recombinant methionyl human granulocyte colony-stimulating factor (r-metHu-G-CSF) produced by recombinant DNA technology using the bacterium strain E.coli K802. It has a molecular weight of approximately 18.8 kDa and is composed of 175 amino acids. The endogenous human G-CSF is glycosylated and does not have the additional methionine amino acid residue in its NH₂-terminal end.

The product is a sterile, clear, colorless, preservative-free solution containing tbo-filgrastim, glacial acetic acid, sorbitol, polysorbate 80, sodium hydroxide, and Water for Injection. The product is available in single-use prefilled syringes that contain either 300 mcg or 480 mcg of tbo-filgrastim at a fill volume of 0.5 mL or 0.8 mL, respectively. See table below for product composition of each single-use prefilled syringe.

<table>
<thead>
<tr>
<th>Product Composition</th>
<th>Tbo-filgrastim</th>
<th>Glacial Acetic Acid</th>
<th>Polysorbate 80</th>
<th>Sorbitol</th>
<th>Sodium Hydroxide</th>
<th>Water for Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mcg/0.5 mL Syringe</td>
<td>300 mcg</td>
<td>0.3 mg</td>
<td>0.0275 mg</td>
<td>25 mg</td>
<td>q.s. to pH 4.2</td>
<td>q.s. to 0.5 mL</td>
</tr>
<tr>
<td>480 mcg/0.8 mL Syringe</td>
<td>480 mcg</td>
<td>0.48 mg</td>
<td>0.044 mg</td>
<td>40 mg</td>
<td>q.s. to pH 4.2</td>
<td>q.s. to 0.8 mL</td>
</tr>
</tbody>
</table>

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Tbo-filgrastim is a human granulocyte colony-stimulating factor (G-CSF) produced by recombinant DNA technology. Tbo-filgrastim binds to G-CSF receptors and stimulates proliferation of neutrophils. G-CSF is known to stimulate differentiation commitment and some end-cell functional activation, which increases neutrophil counts and activity.

12.2 Pharmacodynamics

In the clinical trials of patients with cancer, the time to the ANCmax was between 3 to 5 days and returned to baseline by 21 days following completion of chemotherapy. In the healthy volunteer trials, doubling the tbo-filgrastim subcutaneous dose from 5 to 10 mcg/kg resulted in a 16%-19% increase in the ANCmax and a 33%-36% increase in the area under the effect curve for ANC.

Cardiac Electrophysiology

At the maximum recommended intravenous dose of 5 mcg/kg, tbo-filgrastim did not prolong the QT interval to any clinically relevant extent.

12.3 Pharmacokinetics

In healthy subjects, the absolute bioavailability of 5 mcg/kg subcutaneous tbo-filgrastim was 33%. Increasing the dose of tbo-filgrastim from 5 to 10 mcg/kg in these healthy subjects resulted in an approximately 200% increase in both the maximum concentration (Cmax) and the area under the curve (AUC0-∞) of the drug.

In the clinical trials of patients with cancer, the AUC and Cmax were greater and more variable compared to healthy volunteers receiving the same dose of tbo-filgrastim subcutaneously. The median time to maximum concentration was between 4 to 6 hours and the median elimination half-life was between 3.2 to 3.8 hours. Accumulation was not observed after repeated dosing.

Pharmacokinetics in Specific Populations

Age: Not evaluated.

Gender: No gender-related differences were observed.

Renal Impairment: Mild renal impairment (creatinine clearance 60 - 89 mL/min) had no effect on tbo-filgrastim pharmacokinetics (N=11). The pharmacokinetic profile in patients with moderate and severe renal impairment has not been assessed.
**How will I receive GRANIX?**

- **GRANIX is given by an injection under your skin (subcutaneous) by a healthcare provider.** Your healthcare provider may decide injections can be given at home by you or your caregiver. If **GRANIX is given at home,** see the detailed “Instructions for Use” that comes with your GRANIX for information on how to prepare and inject a dose of GRANIX.

- Your healthcare provider will show you and your caregiver how to prepare and inject GRANIX before you use it.

- Your healthcare provider will tell you how much GRANIX to inject and when to inject it. Do not stop using GRANIX or change your dose unless your healthcare provider tells you to.

- **GRANIX injections are usually given 1 time each day until your white blood cell count returns to normal.**

- Your first dose of GRANIX is given at least 24 hours after you receive your chemotherapy.

- Do not inject GRANIX within 24 hours before your next dose of chemotherapy.

- Your healthcare provider will test your blood before your chemotherapy and during treatment with GRANIX until your white blood cell count returns to normal.

**What are the possible side effects of GRANIX?**

**GRANIX can cause serious side effects, including:**

- **Spleen rupture.** Your spleen may become enlarged and can rupture. A ruptured spleen can cause death. Call your healthcare provider right away if you have pain in your left upper stomach (abdomen)-area or your left shoulder during treatment with GRANIX.

- **A serious lung problem called acute respiratory distress syndrome (ARDS).** Call your healthcare provider or get emergency medical help right away if you have shortness of breath with or without fever, trouble breathing, or a fast rate of breathing.

- **Serious allergic reactions.** GRANIX can cause serious allergic reactions. These reactions can cause a rash over your whole body, shortness of breath, wheezing, dizziness, swelling around your mouth or eyes, fast heart rate, and sweating. If you have any of these symptoms, stop using GRANIX and call your healthcare provider or get emergency help right away.

- **Sickle cell crisis.** You may have a serious sickle cell crisis if you have a sickle cell disorder and use GRANIX. Serious sickle cell crisis has happened in people with sickle cell disorder receiving filgrastim that has sometimes led to death. Call your healthcare provider and your sickle cell provider receiving filgrastim that has sometimes led to death.

- **Kidney injury (glomerulonephritis).** GRANIX can cause kidney injury. Call your healthcare provider right away if you develop any of the following symptoms:
  - swelling of your face or ankles
  - blood in your urine or dark colored urine
  - you urinate less than usual

- **Capillary Leak Syndrome.** GRANIX can cause fluid to leak from blood vessels into your body’s tissues. This condition is called “Capillary Leak Syndrome” (CLS). CLS can quickly cause you to have symptoms that may become life-threatening. Get emergency medical help right away if you develop any of the following symptoms:
  - swelling or puffiness and are urinating less than usual
  - trouble breathing
  - swelling of your stomach-area (abdomen) and feeling of fullness
  - dizziness or feeling faint
  - a general feeling of tiredness

Your healthcare provider may decrease your dose, temporarily stop, or permanently stop treatment with GRANIX if you have certain side effects. The most common side effect of GRANIX is bone pain.
Tell your healthcare provider right way if you have any signs of infection during treatment with GRANIX such as fever, redness, or swelling. These are not all the possible side effects of GRANIX. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store GRANIX?
- Store GRANIX in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store GRANIX in the original carton to protect it from light.
- Do not shake.
- Take GRANIX out of the refrigerator 30 minutes before use and allow it to reach room temperature before preparing an injection.
- GRANIX can be left at room temperature for up to 5 days. If not used within 5 days, return GRANIX back to the refrigerator. Throw away (dispose of) GRANIX that has been left at room temperature for more than 5 days.
- After you inject your dose, throw away (dispose of) any unused GRANIX left in the syringe. Do not save unused GRANIX in the syringe for later use.

Keep GRANIX and all medicines out of the reach of children.

General information about the safe and effective use of GRANIX
Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use GRANIX for a condition for which it was not prescribed. Do not give GRANIX to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about GRANIX that is written for health professionals.

What are the ingredients in GRANIX?
Active ingredient: tbo-filgrastim
Inactive ingredients: glacial acetic acid, sorbitol, polysorbate 80, sodium hydroxide, and Water for Injection

Manufactured by: Sincor Biotech UAB
Distributed by: Teva Pharmaceuticals USA, Inc.
Vilnius, Lithuania North Wales, PA 19454
U.S. License No. 1803 Product of Israel

This Patient Information has been approved by the U.S. Food and Drug Administration
Revised: 02/2017

Instructions for Use
GRANIX (GRAN-icks) (tbo-filgrastim) injection, for subcutaneous use
Important: Keep the GRANIX syringe out of the reach of children.

About the GRANIX syringe
Depending on the prescription that your healthcare provider gave you, you will receive a syringe that provides a dose of either 0.1mL to 0.5mL or 0.1mL to 0.8mL. If you are prescribed a dose over 0.8mL, two syringes will be required to reach your prescribed dose. Your healthcare provider will determine how many syringes and the correct dose in milliliters (mL) you will need to give based on your body weight. You should continue to give GRANIX daily until your healthcare provider informs you that your white blood cell count has returned to normal.

Make sure you understand the following:
• How to store your syringes.
• How to read the syringe markings.
• How to adjust the amount of GRANIX in the syringe for your prescribed dose.
• How to prepare and give the injection.

Do not shake syringes.
Do not remove the needle cap until you are ready to inject.
Do not re-use a syringe. The syringe is for single-use only.
Your first dose of GRANIX is given at least 24 hours after you receive your chemotherapy.
Do not inject GRANIX within 24 hours before your next dose of chemotherapy.

Dosing schedule
Inject your total daily dose 1 time each day as prescribed by your healthcare provider, starting at least 24 hours (1 day) after the end of your chemotherapy cycle. You should continue to give GRANIX daily until your white blood cell count returns to normal.

How to store your GRANIX syringes
- Store GRANIX in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store GRANIX in the original carton to protect it from light.
- Do not shake.
- Take GRANIX out of the refrigerator 30 minutes before use and allow it to reach room temperature before preparing an injection.
- GRANIX syringes can be left at room temperature for a single period of up to 5 days, and if not used can be returned to the refrigerator. Throw away (dispose of) any unused GRANIX syringes that have been left at room temperature for more than 5 days.
- After you inject your dose, throw away (dispose of) any unused GRANIX left in the syringe. Do not save unused GRANIX in the syringe for later use.

Keep GRANIX and all medicines out of the reach of children.
Determining how many syringes you need for your daily dose
• If your prescribed daily dose is 0.5mL or less, use 1 syringe.
• If your prescribed daily dose is 0.8mL or less, use 1 syringe.
• If your prescribed daily dose is more than 0.8mL you will need to prepare 2 syringes in order to match your prescribed dose:
  ◦ Adjust your first syringe to 0.8mL.
  ◦ Adjust your second syringe to the additional amount required to make up your total prescribed dose.
  ◦ Make sure the amounts in both syringes add up to your prescribed dose (See the table to the right to determine how much medicine should be in each syringe).

For example: If your prescribed dose is 1mL you would prepare 1 syringe with 0.8mL and a second syringe with 0.2mL.

Important: When using two syringes always adjust the first syringe to 0.8mL.

How to read the syringe markings
What the markings on the syringe mean:
The syringe is labeled in 0.1mL unit increments from 0.1mL to 0.8mL. There is a line next to each 0.1mL unit increment. To read the dose scale always hold the syringe with the needle-end facing up so that 0.1mL is at the top and 0.8mL is at the bottom.

Do not use the top of the cone or the middle or lower edges of the grey stopper to measure your dose.

Injection procedure (follow the steps below for each day of dosing)
1. Prepare for injection
1A Each time you inject a dose gather the following supplies:
• GRANIX syringe(s)
• Alcohol swabs
• Paper towel
• Cotton ball or gauze
• Bandage (optional)
• Sharps container (hard-walled container for discarding syringes)

Note: GRANIX and all of the parts of the prefilled syringe do not contain natural rubber latex.

1B Take the carton with the syringe(s) out of the refrigerator
1C Check the label and the expiration date on the side of the carton
1D Remove the syringe(s) from the carton
Open the carton by breaking the tamper proof seal and lifting the lid. Remove the number of syringes required for your daily dose by grasping each at the middle of the syringe body.
After removing your required number of syringes, place the carton back in the refrigerator.

1E Look carefully at the syringe(s) and the medicine
Hold the syringe body and check to make sure it is not damaged. Inspect the medicine in the syringe. GRANIX should be a clear liquid.

Important: Do not inject if:
• GRANIX® (tbo-filgrastim) is not listed on the syringe label.
• The medicine is cloudy, discolored, or foamy.
• The medicine contains lumps, flakes, or particles.

1F Wait 30 minutes for the syringe(s) to warm to room temperature
Wait 30 minutes for GRANIX to naturally warm to room temperature. This will provide a more comfortable injection.

1G Wash your hands
When ready to inject, wash your hands with soap and warm water and dry thoroughly with a clean towel.

1H Choose an injection site
The recommended injection sites are:
If you are self-injecting:
Stomach-area (abdomen): Except for a 2-inch area around the navel (belly button).
Thighs: Top or middle area of thighs.
If a caregiver is injecting GRANIX for you:
Arms: Fleshy areas on upper, back part of the arm.
Upper hip or buttock: Fleshy areas around the back of the upper hips and upper sides of the buttocks.
If 2 injections will be performed, then the second injection should be at least 1 inch away from the first injection.

Do not inject into areas that are tender, red, bruised, hard, or have scars or stretch marks.
Important:
• You should select a different injection site each time you give yourself an injection.
• If you want to use the same injection site for a dose requiring 2 injections, make sure the second injection site is at least 1 inch away from the first injection site.

1I Clean the injection site using an alcohol swab
Allow site to dry for 5-10 seconds to avoid stinging.
If giving 2 injections, then the distance between the 2 injection sites should be at least 1 inch apart.

2A Remove the needle cap from the syringe
Place a paper towel on the table.
To remove the needle cap, hold the body of the syringe firmly with 1 hand (with the needle facing away from you).
Pull the needle cap straight off, extending your hand away from the needle.

Note: Throw away the needle cap in a sharps container.
Do not recap the needle now or after the injection.

2B Hold the syringe upright and tap
Hold the syringe upright (needle pointing up), as shown.
Gently tap the barrel with your fingers to make sure any air bubbles rise to the top.

2C Slowly and carefully adjust the medicine level
Hold the syringe with the needle pointing up and slightly away from you, as shown. Make sure you can easily see the syringe markings and numbers. Holding the plunger as shown, very slowly and carefully push the plunger up until the top edge of the grey rubber stopper is even with the line that corresponds to your prescribed dose.

Note:
• If GRANIX gets on your skin, wash your skin with soap and water.
• If GRANIX get in your eyes, flush well with water.
GRANIX® (tbo-filgrastim) injection

3. INJECT MEDICATION

3A Pinch skin

Note: If you accidentally removed too much GRANIX, contact your healthcare provider before giving your injection.

3B Insert the needle at a 45 to 90 degree angle

Hold the body of the syringe between your thumb and index finger. Use a quick motion to fully insert the needle straight into the pinched skin at a 45 to 90 degree angle.

When the needle is inserted, you can release the pinched skin.

Do not hold or push on the plunger while inserting the needle into the skin.

3C Push the plunger down injecting all of the GRANIX

Use your finger to gently push down on the plunger. When the plunger head is as far down as it will go, all of the GRANIX has been injected. When done, gently remove the needle from the skin.

3D Dispose of used syringe

Put your used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes in your household trash.

If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: http://www.fda.gov/safesharpsdisposal.

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

3E Treat the injection site if needed and wash your hands

If you see drops of blood at the injection site, you can press a cotton ball or gauze over the injection site for several seconds to stop the bleeding. Apply bandage, if needed.

When you are finished, wash your hands with soap and warm water and dry thoroughly with a clean towel.

4. Repeat the procedure with the second syringe (If dose is more than 0.8mL)

If your dose is more than 0.8mL:

- Follow instructions 3A through 3E for injecting.
- Choose a different site for your second injection. If you want to use the same part of your body, make sure the second injection site is at least 1 inch away from the first injection site.