

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

Pr **Grastofil**[®] (pronounced) GRAS-toh-fill **filgrastim Injection**

Read this carefully before you start taking **Grastofil**[®] and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Grastofil**[®].

Grastofil[®] is a biosimilar biologic drug (biosimilar) to the reference biologic drug Neupogen. A biosimilar is authorized based on similarity to a reference biologic drug that was already authorized for sale.

Serious Warnings and Precautions

- Your spleen may become enlarged and rupture while taking **Grastofil**[®]. A ruptured spleen can cause death. Call your doctor right away if you or your child has pain in the left upper stomach area, or left shoulder tip area.
- If you have sickle cell trait or sickle cell disease, make sure that you tell your doctor before you start taking **Grastofil**[®] so that the potential risks and benefits can be discussed. In patients with sickle cell trait or sickle cell disease, severe sickle cell crises have been associated with the use of filgrastim, resulting in death in some cases.

What is **Grastofil[®] used for?**

Grastofil[®] is used to treat neutropenia (nu-tro-**peen**-ee-ah), a condition where the body makes too few neutrophils. Neutropenia may be a long-standing condition where your body does not make enough neutrophils, or it may be caused by drugs used to treat cancer. In some cases, your body may make enough neutrophils, but as a part of your treatment for cancer, your doctor may want to increase the number of certain blood cells (CD34 cells) and collect them. The cells are collected using a process called apheresis (ay-fer-**ree**-sis). These collected cells are given back to you after you receive very high doses of treatment for cancer to make your blood counts get back to normal more quickly.

How does **Grastofil[®] work?**

Grastofil[®] is a man-made form of granulocyte colony stimulating factor (G-CSF), which is made using the bacteria *E coli*. G-CSF is a substance naturally produced by the body. It stimulates the growth of neutrophils (**nu**-tro-fils), a type of white blood cell important in the body's fight against infection. **Grastofil**[®] works by helping the body make more neutrophils. To make sure **Grastofil**[®] is working, your doctor will ask that you have regular blood tests to count the number of neutrophils you have. It is important that you follow your doctor's instructions about getting these tests.

What are the ingredients in **Grastofil[®]?**

Medicinal ingredients: filgrastim

Non-medicinal ingredients: acetate, polysorbate 80, sodium, sorbitol (E420), and water for injection. The pre-filled syringe components contain natural rubber (a derivative of latex), which should not be handled by persons sensitive to this substance.

****Grastofil**[®] comes in the following dosage forms:**

Grastofil[®] is available in single-use graduated (1/40 graduations from 0.1 mL to 1.0 mL) pre-filled syringes with an UltraSafe Plus[™] Passive Needle Guard, as a clear, colourless injection in two sizes of 300 mcg/0.5mL and 480 mcg/0.8 mL (both containing 600 mcg/mL of filgrastim). These are available in cartons of 1 and 10 individually blistered pre-filled syringes per carton.

Do not use Grastofil® if:

- You are allergic (hypersensitive) to filgrastim or any of its ingredients. For a detailed list of medicinal and nonmedicinal ingredients, see above “**What are the ingredients in Grastofil®?**”.
- You are allergic to other medicines made using the bacteria *E.coli*. Ask your doctor if you are not sure.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Grastofil®. Talk about any health conditions or problems you may have, including if you:

- Get left upper abdominal pain or pain at the tip of your shoulder,
- Have osteoporosis (loss of calcium from the bones which leads to the bones becoming weak and fragile),
- Are suffering from any other illness (especially if you think you may have an infection),
- Experience a cough, fever and difficulty breathing,
- Have sickle cell trait or sickle cell disease (an inherited blood disorder that affects red blood cells),
- Are taking or have recently taken any other medicines, including medicines obtained without a prescription,
- Are breast-feeding,
- Are pregnant, or think you may be pregnant or plan to get pregnant.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Grastofil®:

Interactions between Grastofil® and other drugs have not been studied. Drugs such as lithium may affect the release of neutrophils into your blood stream. You should discuss your treatment with your doctor before using Grastofil®.

How to take Grastofil®:

If you/your child are receiving Grastofil® because you are also receiving chemotherapy, the last dose of Grastofil® should be injected at least 24 hours before your next dose of chemotherapy.

Usual dose:

Your doctor will determine your/your child’s correct dose based on your/your child’s body weight.

Overdose:

You must always use the correct dose of Grastofil®. Too little Grastofil® may not protect you against infections, and too much Grastofil® may cause too many neutrophils to be in your blood.

If you think you have taken too much Grastofil®, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.
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Missed Dose:

Grastofil® should be injected at the same time each day. If you miss a dose contact your doctor or nurse.

Information on How to Inject Grastofil®:

This section contains information on how to give an injection of Grastofil®. **It is important that you do not try to give the injection unless you have received training from your doctor or nurse.** If you are not sure about giving the injection or you have any questions, please ask your doctor or nurse for help.

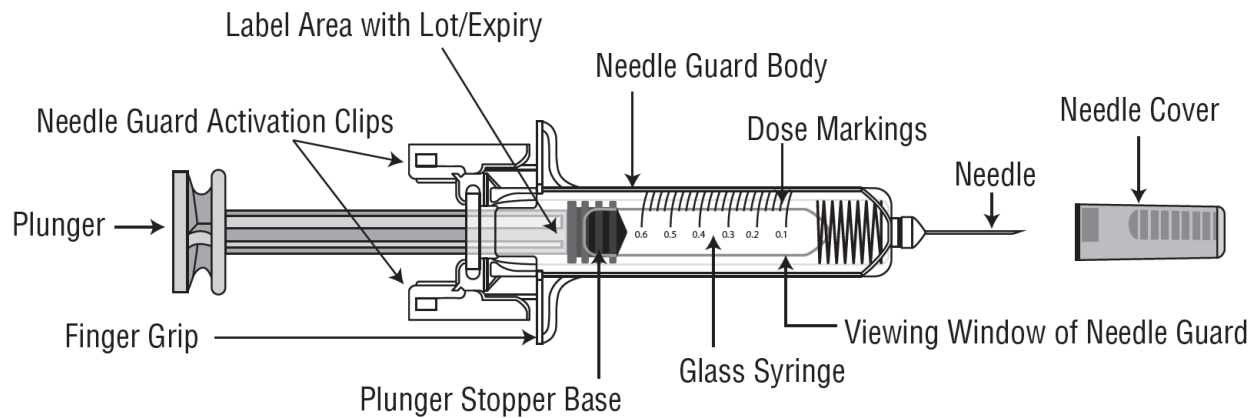
Injecting with Grastofil®:

You will need to give an injection into the tissue under the skin, known as a subcutaneous injection. Your doctor or nurse will tell you how frequently it should be injected.

Before Injecting Grastofil®:

To give a subcutaneous injection you will need:

1. A new pre-filled syringe of Grastofil® with an UltraSafe Plus™ Passive Needle Guard.



2. Alcohol wipes or similar.
3. Cotton or gauze.
4. A puncture-proof container for disposing of used syringes, as discussed with your doctor/nurse.

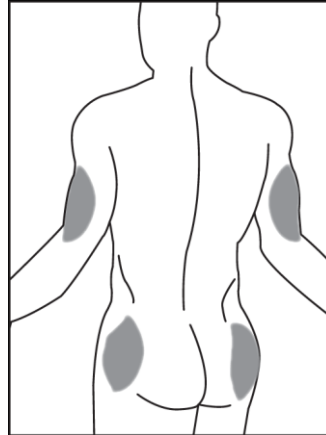
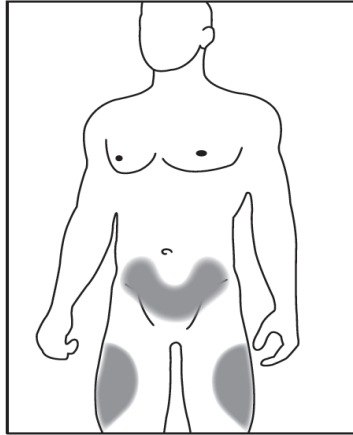
Setting-up for the Injection:

1. Remove one Grastofil® pre-filled syringe in the blister packaging from the refrigerator and leave it unopened on your working surface for about 30 minutes so that it reaches room temperature. Confirm on the syringe and carton that it is the correct dose (300 mcg/0.5 mL or 480 mcg/0.8 mL Grastofil®) as prescribed by your doctor.
2. Check the expiry date which is stated on the carton and syringe label (see EXP). Do not use it if the date has passed the last day of the month shown.
3. Do not shake the pre-filled syringe as vigorous shaking may damage the medication. Check the appearance of Grastofil®. It must be clear. If it is cloudy or there are particles in it, you must not use it.
4. Clean your hands thoroughly with soap and water and/or hand sanitizer.
5. Find a comfortable, well-lit place and put the syringe, the alcohol wipes, cotton or gauze, and the puncture-proof container where you can reach them.
6. Keep the needle cover on the needle until you are ready to inject or measure your dose and inject.

Choosing an Injection Site:

The most suitable injection sites (places on your body) to inject Grastofil® are:

- The outer area of your upper arms
- The front of your middle thighs
- The abdomen, **except for the 2 inches area around the navel**
- Upper outer area of your buttocks



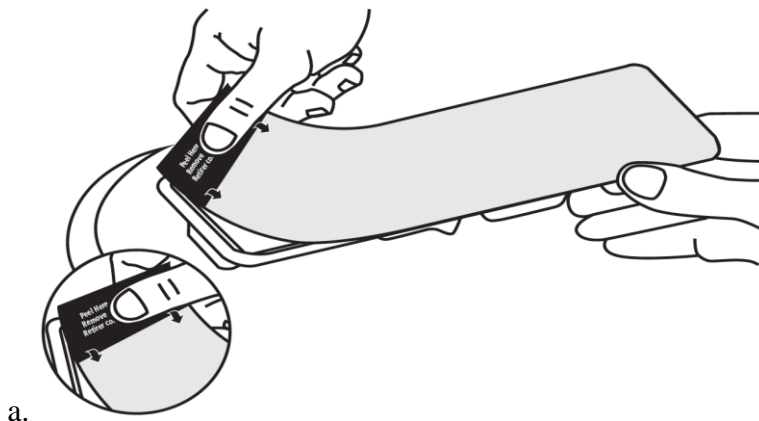
From the above options, change the injection site each time you take an injection so that you do not develop soreness in one area. Do not inject into the same site that is tender, red, bruised or hard or that has scars or stretch marks.

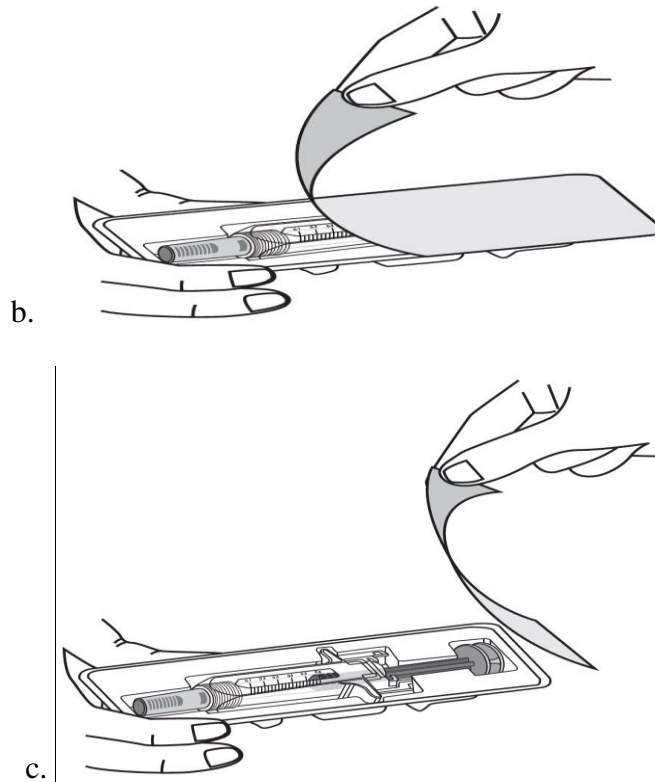
How do I give my injection?

IMPORTANT: REMOVAL OF INDIVIDUAL SYRINGE FROM BLISTER PACKAGING

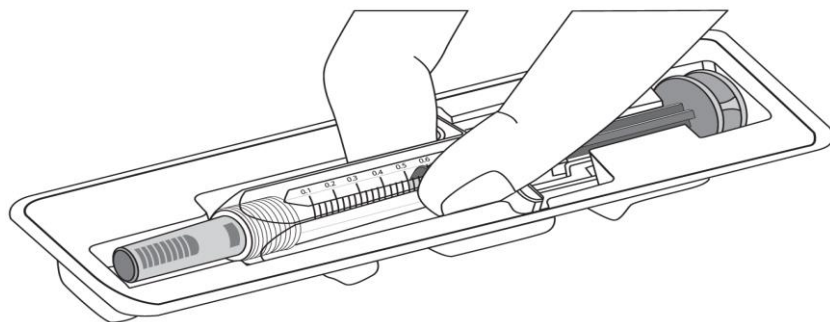
Follow directions for correct handling technique as shown below when removing the pre-filled syringe with the UltraSafe Plus™ Passive Needle Guard from the packaging, otherwise, the needle's safety mechanism may be triggered, making the syringe unusable.

1. Locate the end of the blister packaging with the stripe as indicated by the 2 arrows and “Peel Here” on the top layer. From this end, open the blister pack by peeling back the top layer **COMPLETELY OFF**.

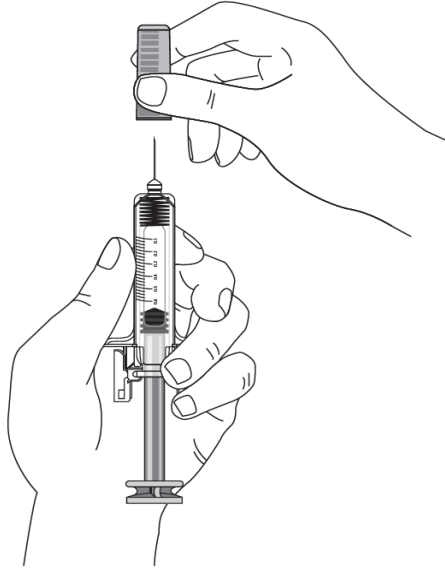




2. Remove the syringe from the blister pack **by the body** as shown below. **Do not** lift the product by the plunger or needle cover. **Do not** touch the needle guard activation clips at any time during use. This may trigger the needle's safety mechanism causing the needle to retract (pull back) before your injection is given. This will make the syringe unusable.



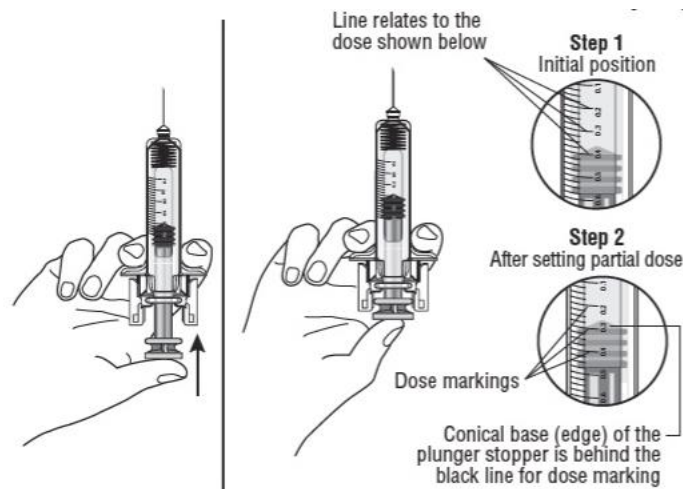
3. You must **always clean** the skin on the selected injection site by using an alcohol wipe.
4. Hold the pre-filled syringe by the body (needle guard) with the needle pointing up and avoid touching the needle guard activation clips. Holding the syringe by the body with the needle pointing up helps to prevent the medicine from leaking out of the needle. **Carefully pull the needle cover straight off without twisting it. Do not touch the needle or plunger. Do not use if the syringe is damaged or needle is bent.** If the syringe is damaged or needle is bent, throw away (dispose of) the syringe in the puncture-proof container.



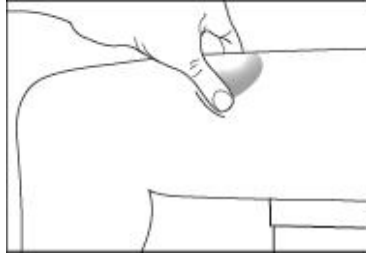
For patients injecting the full content of your syringe (as prescribed by your doctor), proceed to Step 5.

For patients injecting a partial dose only (as prescribed by your doctor): Holding the pre-filled syringe as shown in the image below, press slowly on the plunger to push out the excess medicine until the conical base of the plunger stopper lines up with the syringe marking for your prescribed dose.

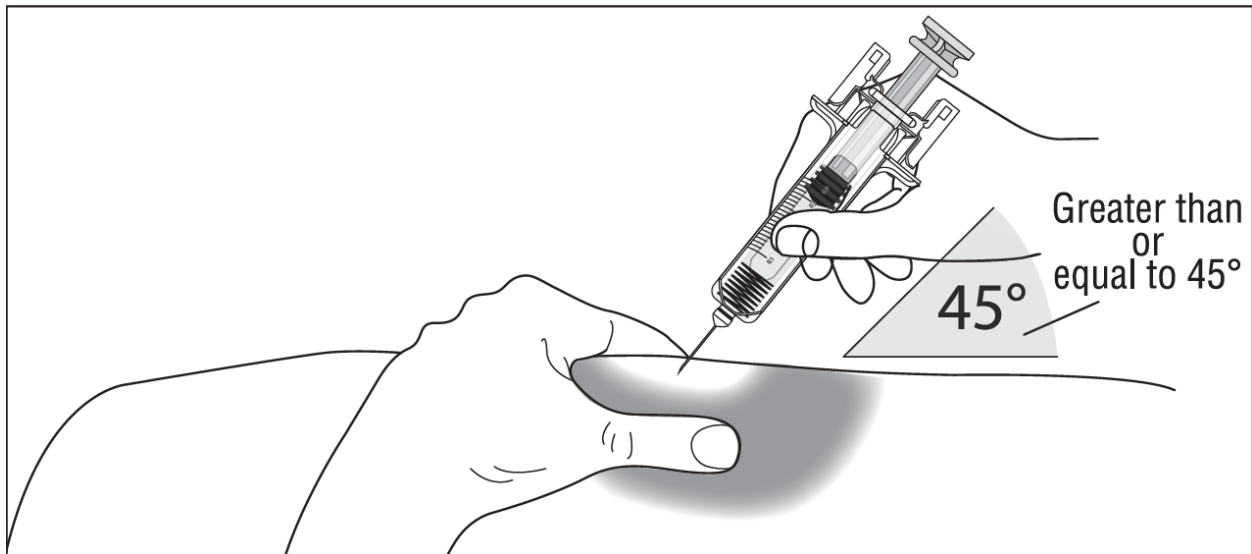
Check again to make sure the correct dose of Grastofil® is in the syringe.



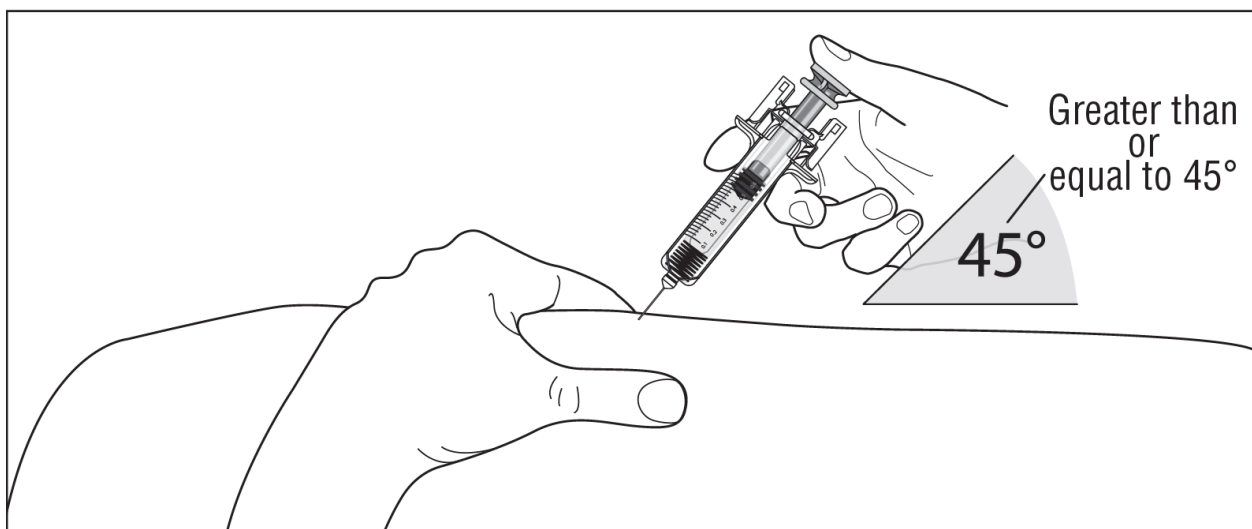
5. Hold the pre-filled syringe between the thumb and forefinger of the hand you will use to inject Grastofil®. Use the other hand to pinch a fold of the skin at the cleaned injection site between your thumb and forefinger, without squeezing it as shown below.



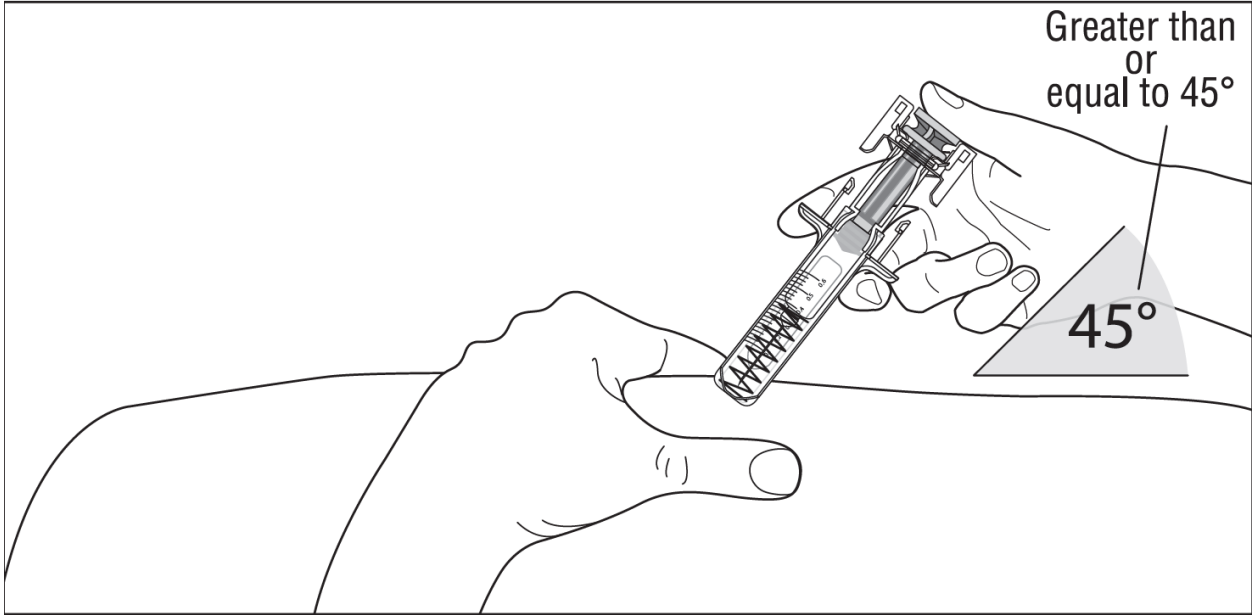
6. Insert the needle under the skin at an angle of approximately greater than or equal to 45° as shown by your doctor or nurse.



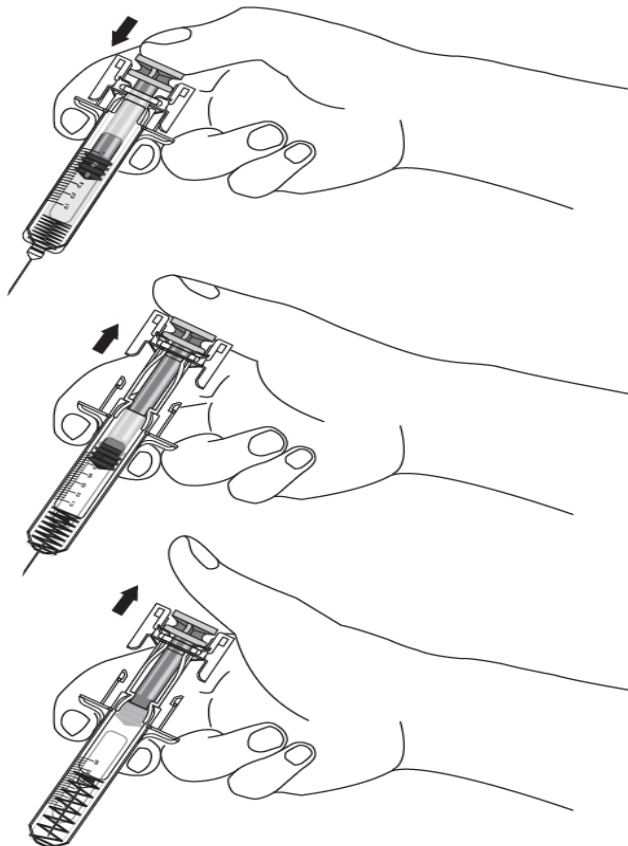
7. After the needle is inserted, let go of the fold of the skin. Inject the prescribed dose by pushing the plunger with your thumb while grasping the finger grips as shown in the image below and as directed by your doctor or nurse.



8. Press the plunger slowly and completely, until all of the medication has been injected as shown below. The needle guard will not be activated unless the entire dose has been administered and you remove downward pressure on the plunger.



When the syringe is emptied of all the medication, slowly lift your thumb from the plunger which will release the needle-guard. The needle will then withdraw from the skin and be covered and locked in place by the needle-guard.



9. After the injection, immediately place cotton or gauze on the injection site and apply pressure for several seconds. Do not use Grastofil® that is left in the syringe.

10. Place the pre-filled syringe with the needle guard covered needle into a puncture-proof container for proper disposal as described below. Use each pre-filled syringe only for one injection.

Remember:

Do not hesitate to consult your doctor or nurse for help or if you have any concerns.

Disposal of Used Syringes:

The used syringes should be disposed of in accordance with local requirements.

- Put used syringes into an appropriate puncture-proof container as instructed by your doctor/nurse.
- **Always** keep this container **out of reach and sight of children**.
- When the puncture-proof container is full, it should be disposed as instructed by your doctor, nurse or pharmacist. **Do not throw the container in the household trash. Do not recycle.**
- Never put used syringes into your normal household waste bin.

What are possible side effects from using Grastofil®?

These are not all the possible side effects you may feel when taking Grastofil®. If you experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions. Like all medications, Grastofil® may show side effects upon use and based on individual response.

Spleen Rupture: Your spleen may become enlarged and can rupture while taking Grastofil®. A ruptured spleen can cause death. The spleen is located in the upper left section of your stomach area. Call your doctor right away if you or your child has pain in the left upper stomach area or left shoulder tip area. This pain could mean you or your child's spleen is enlarged or ruptured.

Serious Allergic Reactions: Grastofil® can cause serious allergic reactions. These reactions can cause body rash, shortness of breath, wheezing, dizziness, swelling, fast pulse, and sweating. If you or your child starts to have any of these symptoms, stop using Grastofil® and call your doctor or seek emergency care right away. If you or your child has an allergic reaction during the injection of Grastofil®, stop the injection right away.

A serious lung problem called acute respiratory distress syndrome (ARDS): Call your doctor or seek emergency care right away if you or your child has shortness of breath, trouble breathing or a fast rate of breathing.

Sickle Cell Crisis: Call your doctor or seek emergency care right away if you or your child experiences severe pain in the bones, chest, gut or joints.

Kidney injury (glomerulonephritis): Call your doctor right away if you experience puffiness in your face or ankles, blood in your urine or brown coloured urine, or if you notice that you urinate less often than usual.

The common side effects of use of Grastofil® are: The most common side effect you/your child may experience is bone, joint and muscle pain. This pain can be relieved by taking a non-acetylsalicylic acid pain reliever such as acetaminophen.

In addition, other common side effects can be fatigue, headache, loss of appetite, diarrhea, cough, sore throat, elevation in liver enzymes, reduction in platelets (cells involved in clotting), which increases the risk of bleeding or bruising.

Some people may experience a lump, redness, swelling, bruising or itching at the site of injection. This may be an allergy to the ingredients or could be a local reaction. **If at any time a serious allergic reaction occurs, immediately call the doctor or emergency services (for example, call 911).**

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON: ≥ 10% Bone pain		√	
COMMON: ≥ 1% and < 10% Splenomegaly (including the following symptoms: pain in the left upper stomach area or left shoulder tip area)		√	
Osteoporosis in children with severe chronic neutropenia (including decreased bone density, making them weak, more brittle and likely to break)		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
UNCOMMON: $\geq 0.1\%$ and $< 1\%$ Splenic rupture (including the following symptoms: left upper abdominal pain or pain at the tip of your shoulder) Capillary Leak Syndrome (including the following symptoms: 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)		√	√
		√	√
RARE: ≥ 0.01 and $< 0.1\%$ Allergic reactions [body rash, shortness of breath, a drop in blood pressure (usually causing dizziness or light headedness), swelling around the mouth or eyes, fast pulse, weakness, sweating, severe redness or swelling or itching at injection site] Acute respiratory distress syndrome (including the symptoms: fever, shortness of breath, cough, or congestion in your lungs) Cutaneous Vasculitis (including the following signs: inflammation of the blood vessels in the skin) Sweet's Syndrome (including the following symptoms: plum-coloured, raised, painful sores on the limbs and sometimes the face and neck with a fever)		√	√
		√	√
		√	√
		√	√
VERY RARE: $< 0.01\%$ Alveolar hemorrhage and hemoptysis (including the following symptoms: bleeding from the lungs and coughing of blood) Pseudogout (including the following symptoms in patients treated for cancer: pain and swelling of the joints, similar to gout)		√	√
		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on [Adverse Reaction Reporting](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax, or;
- Calling 1-866-234-2345;

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Do not use Grastofil® after the expiry date which is stated on the outer carton and on the pre-filled syringe.

- Store in a refrigerator (2°C to 8°C). Do not freeze. Do not shake.
- If Grastofil® is accidentally frozen, allow it to thaw in the refrigerator before giving the next dose. However if it is frozen for a second time, do not use it and contact your doctor or nurse for further instructions.
- Grastofil® can be removed from the refrigerator and left at room temperature (not above 25°C) for a single period of up to 15 days that ends within the labelled expiry date. Once Grastofil® has been out at room temperature it should not be put back into the refrigerator. Any Grastofil® syringes that have been out of the refrigerator for longer than 15 days should not be used and should be disposed of in accordance with local requirements.
- Keep the pre-filled syringe in the carton in order to protect from light. Do not use if you notice it is cloudy or there are particles in it.

Medicines should not be disposed via wastewater or household waste. Ask your pharmacist how to dispose medicines no longer required. These measures will help to protect the environment.

Keep out of reach and sight of children.

If you want more information about Grastofil®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](http://hc-sc.gc.ca/index-eng.php) (<http://hc-sc.gc.ca/index-eng.php>). Find the Patient Medication Information on the manufacturer's website <http://www.apotex.ca/products>, or by contacting DISpedia, Apotex's Drug Information Service at: 1-800-667-4708

This leaflet was prepared by Apotex Inc., Toronto, Ontario, M9L 1T9.

UltraSafe Plus™ Passive is a trademark of Safety Syringes, Inc., parent company is Becton, Dickinson and Company.

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