

HOW TO INJECT BESREMI[®]

INSTRUCTIONS FOR USE

BESREMI[®]
(ropeginterferon alfa-2b)
Injection, for subcutaneous use

Single-use pre-filled syringe

Read this Important Safety Information carefully. It explains the serious risks of BESREMI[®] and how to take it safely. Talk to your healthcare provider if you have any questions.

What is the most important information I should know about BESREMI[®]?

Interferons, including BESREMI[®], cause or aggravate fatal or life-threatening neuropsychiatric (mental illness), autoimmune (where the body's immune system attacks the body's own cells), ischemic (conditions in which blood flow, and thus oxygen, is restricted to a part of the body) and infectious disorders. If you have persistently severe or worsening signs or symptoms of these conditions you should contact your doctor. Your doctor will assess you and may discontinue you from therapy. In many cases, but not all cases, these disorders resolve after stopping interferon therapy.

This brochure is intended for patients who have been prescribed BESREMI[®] and should be used together with guidance from your healthcare provider.

This Instructions for Use guide is a summary and does not include everything about BESREMI[®]. For complete safety information, including serious warnings and precautions, contraindications, adverse reactions, dosing considerations, and monitoring requirements, please review the additional Important Safety Information on pages 11-13 and the full Patient Medication Information included with the BESREMI[®] carton. If you have questions about BESREMI[®] or how to self-inject, speak with your healthcare provider.

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Your healthcare provider has prescribed **BESREMI®**, an injectable medicine to treat adults with polycythemia vera (PV). This guide covers all you need to know about preparing and injecting **BESREMI®**.

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Watch the instructions for use video

Scan the QR code or visit www.besremi.ca to find out more and watch a video that shows step-by-step instructions on how to prepare and administer BESREMI®.



Still have questions about using BESREMI®?

- Visit www.besremi.ca to get answers to frequently asked questions
- Speak to a ForYOU™ Patient Support Program Nurse Case Manager, at 1-833-4YOU PSP (1-833-496-8777) between 9AM-5PM ET Monday-Friday, or email besremi@foryoupsp.com.

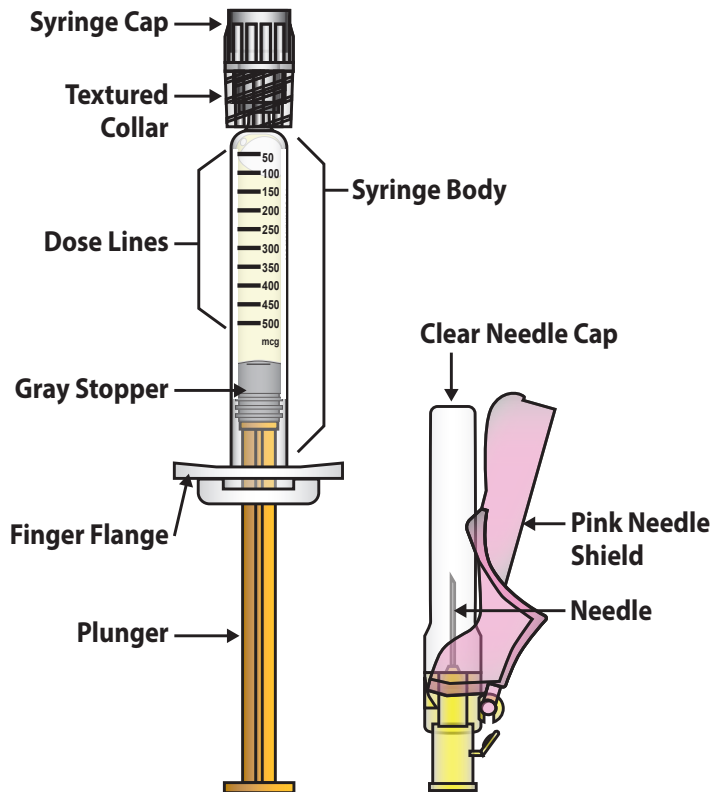
Important information you need to know before injecting with the single-use BESREMI[®] pre-filled syringe.

Read this Instructions for Use guide before using your single-use BESREMI[®] pre-filled syringe and each time you get a new prescription. There may be new information. This leaflet does not take the place of talking with your healthcare provider about your medical condition or your treatment. Ask your healthcare provider about the right way to prepare and give your BESREMI[®] injection.

- Your healthcare provider will tell you the prescribed dose that you should take and the right amount of BESREMI[®] to measure in the pre-filled syringe for your dose. Each time you inject, be sure that you know the prescribed dose of BESREMI[®] to inject. Your dose may change over time.
- BESREMI[®] is for subcutaneous (under the skin) injection only. Do not inject into a vein.
- BESREMI[®] must be injected immediately after preparing the dose.
- BESREMI[®] is for one-time use only. Do not reuse your pre-filled syringe or needle.
- Do not use a pre-filled syringe or needle that is damaged or broken. Contact your healthcare provider for a replacement pre-filled syringe or additional needles.
- Inject BESREMI[®] into the top of the thighs or lower stomach just under the skin. Do not inject BESREMI[®] into any other area of the body.
- Throw away (dispose of) the BESREMI[®] pre-filled syringe with needle attached right away after use.

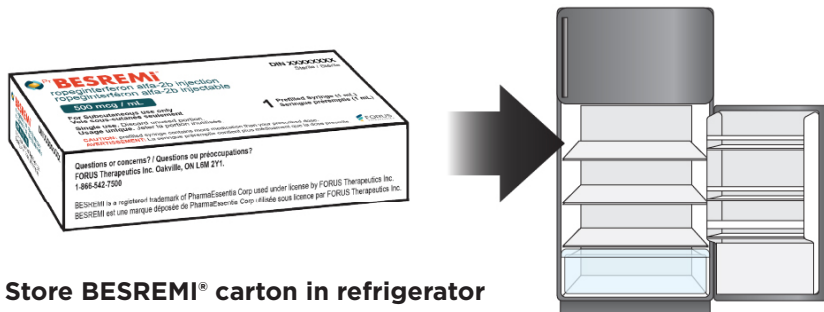
Guide to components and storage

Guide to pre-filled syringe and needle parts



Storing BESREMI®

- Store BESREMI® in a refrigerator at 2°C to 8°C in the original carton to protect from light.
- **Do not** freeze the pre-filled syringes.
- **Do not** use a pre-filled syringe that has been frozen or left in direct sunlight.
- Keep out of reach and sight of children.



Store BESREMI® carton in refrigerator

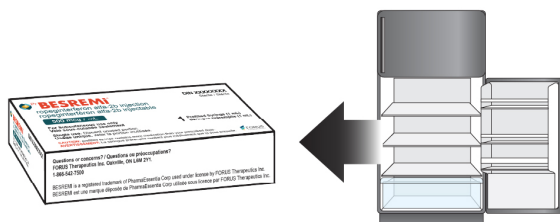
Please see important safety information on pages 11 to 13 of this brochure and speak with your healthcare provider if you have any questions about polycythemia vera or your treatment with BESREMI®.

Gather and check supplies

STEP 1

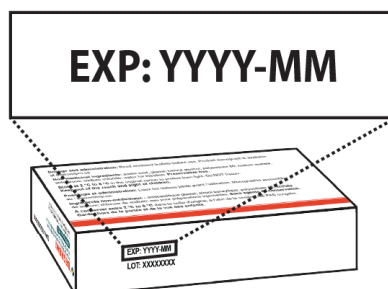
Prepare the BESREMI® pre-filled syringe

- 1.1** Take the BESREMI® carton out of the refrigerator.



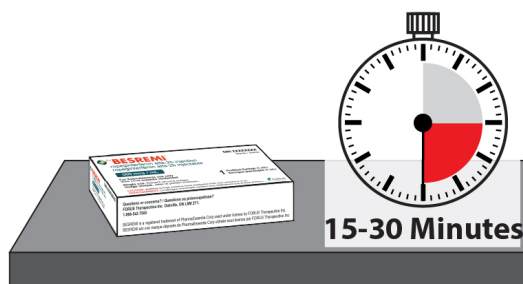
- 1.2** Check the expiration date (“EXP”) on the top panel of the carton to make sure it has not passed.

Do not use the pre-filled syringe if the expiration date has passed.



- 1.3** Let BESREMI® sit on a clean work surface for **15 to 30 minutes** to allow it to come to room temperature.

Do not warm the pre-filled syringe any other way.

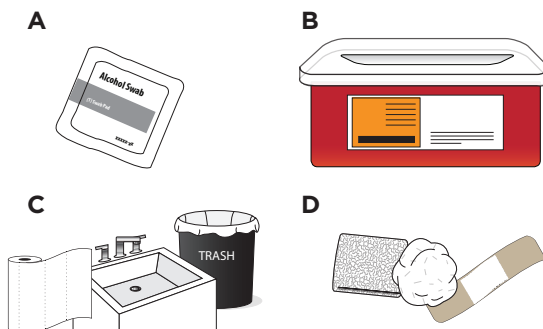


STEP 2

Gather supplies for injection

- 2.1** After allowing the carton to come to room temperature for 15 to 30 minutes, gather the following additional supplies.

- A.** Alcohol swab
- B.** Sharps disposal container
- C.** A paper towel, sink, or trash can to minimize mess during dose adjustment
- D.** Optional items: Gauze or cotton ball and a small adhesive bandage



Gather and check supplies (continued)

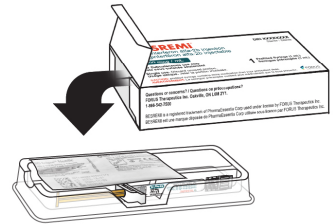
STEP 3

Wash hands and remove syringe from tray

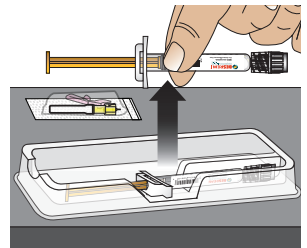
3.1 Wash your hands with soap and water, then dry your hands.



3.2 Open the carton and remove the clear plastic tray that holds the BESREMI® pre-filled syringe and needle package.



3.3 Remove the needle package and BESREMI® pre-filled syringe from the plastic tray. Hold the pre-filled syringe by the middle of the syringe body during removal.



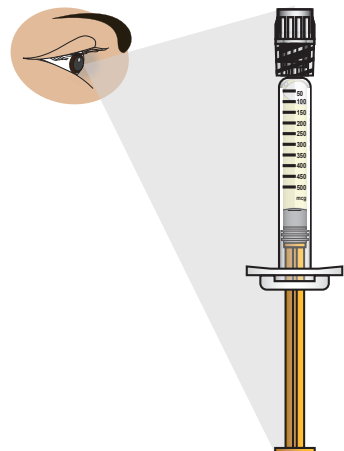
STEP 4

Check the liquid medicine in the BESREMI® pre-filled syringe

4.1 Check the liquid medicine in the pre-filled syringe. The liquid should be clear and colorless to slightly yellow and should not have particles.

Do not use the pre-filled syringe if the liquid is cloudy, discolored, or contains particles. Contact your healthcare provider or pharmacist.

4.2 Check the syringe to see if it is damaged or broken. **Do not** use the pre-filled syringe if it shows any signs of damage or breakage. Contact your healthcare provider or pharmacist.



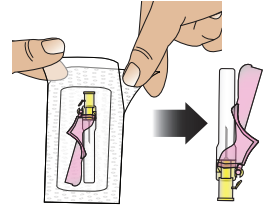
Prepare syringe for injection

STEP 5

Attach the needle to the BESREMI® pre-filled syringe

5.1 Carefully open the needle package, remove the needle, and set it aside.

Throw away the packaging into household trash.

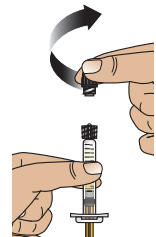


5.2 Hold the pre-filled syringe as shown.

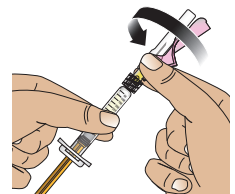
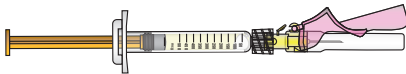
Remove the pre-filled syringe cap by unscrewing it counter-clockwise.

Throw away the syringe cap into household trash.

Do not allow the tip of the pre-filled syringe to touch anything.



5.3 Attach the needle to the pre-filled syringe by firmly pushing it into the collar of the syringe and then screwing it on (turn clockwise) until it feels securely attached. The needle should now be assembled to the pre-filled syringe.



STEP 6

Choose and clean injection site

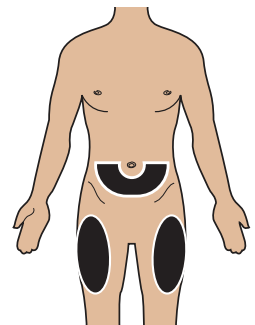
6.1 Choose one of the following injection sites:

- Lower stomach (abdomen) area, at least 2 inches away from the belly button,
- Top of thighs.

Do not inject into skin that is irritated, red, bruised, infected, or scarred.

Do not inject into a vein. BESREMI® is for subcutaneous (under the skin) injection only.

Rotate (change) the injection site for each injection.



6.2 Clean the chosen injection site with an alcohol swab and let it air dry.

Do not blow on or touch the injection site after it has been cleaned.



Prepare syringe for injection (continued)

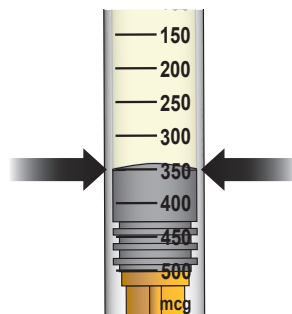
Read
me

How to adjust the medicine level for your prescribed dose

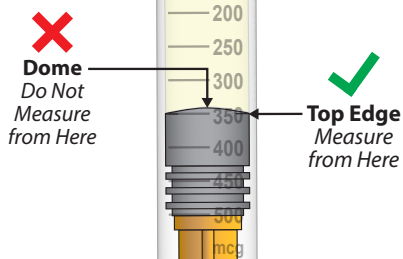
When setting your dose in Step 8, you will need to line up the top outer edge of the gray stopper with the specific dose line and number on the syringe that matches your prescribed dose.

Do not line up the dome (at the top of the stopper) with the dose line.

Align Top Outer Edge of Stopper to Dose Line



Example of 350 mcg dose



Example of 350 mcg dose

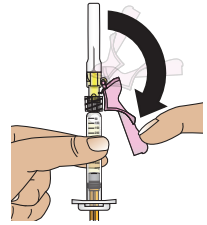
Prepare syringe for injection (continued)

STEP 7

Uncap needle and move air bubbles to top

7.1 Pull the pink needle shield back.

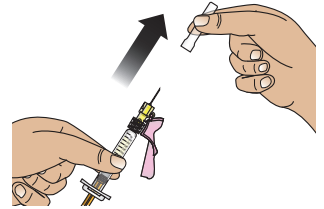
Note: The pink needle shield will be used after the injection to cover the needle and protect from needle-stick injuries.



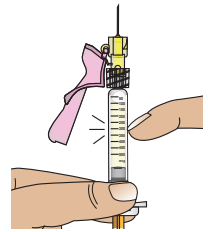
7.2 Hold the syringe from the syringe body. Remove the clear needle cap by pulling it straight off. Throw away the needle cap into household trash.

Do not recap needle.

Tip: When removing the cap, pull it straight off in one smooth motion and keep your fingers away from the needle to help avoid an accidental needle prick.



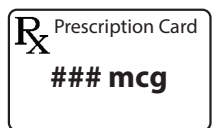
7.3 Hold the pre-filled syringe with the needle pointing up. Tap on the body of the pre-filled syringe to move any air bubbles to the top.



STEP 8

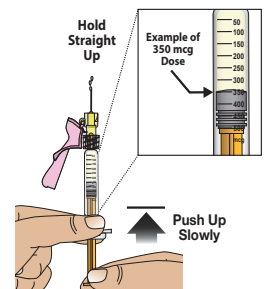
Set your dose

8.1 Check your prescription to identify your prescribed dose. Depending on your prescribed dose, you may have to adjust the dose in the syringe by getting rid of (discarding) some medicine from the pre-filled syringe before you inject the medicine.



8.2 To set your dose follow the four steps below:

- 1. Hold** the pre-filled syringe at eye level with the needle **pointing straight up** over a paper towel, sink, or trash can.
- 2. Check** that you can see the dose lines and number markings on the pre-filled syringe.
- 3. Pinch** the end of the plunger as shown.
- 4. Slowly push up** on the plunger to remove liquid medicine until the top edge of the gray stopper lines up with the marking for **your prescribed dose. Keep holding straight up as you set the dose.**



Important: If you accidentally remove too much liquid medicine, **do not** inject. Contact your healthcare provider or pharmacist.

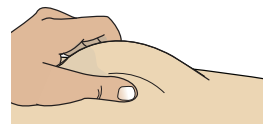
Caution: The example shown may not be your prescribed dose. Always adjust the medicine level in the syringe to match your prescribed dose.

Inject BESREMI®

STEP 9

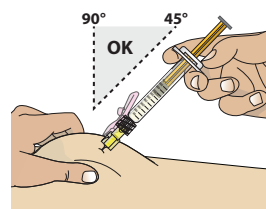
Give Injection

9.1 Pinch the chosen injection site.



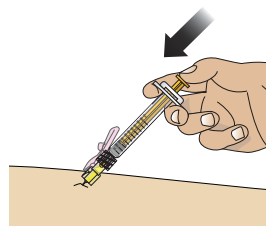
9.2 While pinching the skin, insert the needle at a 45 to 90 degree angle into the pinched skin. Then release the pinched skin.

Tip: When inserting the needle, hold the syringe by the syringe body and keep your fingers away from the plunger. This helps prevent the medication from being released before you are ready to inject.

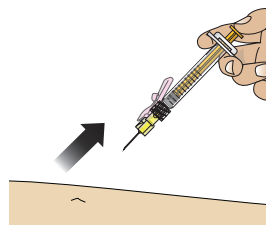


9.3 Inject the medicine by slowly pressing down on the plunger all the way until it stops.

Tip: Confirm the plunger is pushed all the way down to ensure the full dose is delivered.



9.4 After all the liquid medicine is injected, remove the needle from the skin.



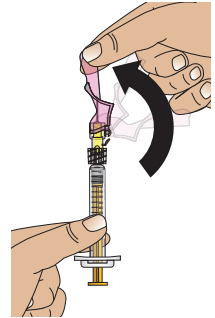
Dispose of used syringe

STEP 10

Cover needle, throw away (dispose of) syringe, and treat injection site

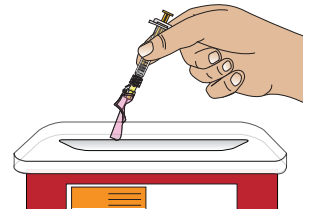
10.1 Carefully push the pink needle shield over the needle until it snaps into place and covers the needle. This helps prevent needle-stick injuries.

Do not recap the needle using the needle cap; only use the pink needle shield to cover the needle.



10.2 Throw away the used pre-filled syringe, with the needle still attached, into a sharps disposal container right away.

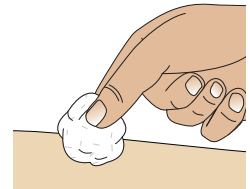
Note: Your sharps container may look different or be a different colour than the one shown in the image.



10.3 If there is a small amount of blood or liquid at the injection site, press a gauze or cotton ball over the injection site until the bleeding stops.

Do not rub the injection site.

If needed, you may apply a small adhesive bandage.



Important safety information

Do not use BESREMI® if:

- you are allergic to ropeginterferon alfa-2b or any of the other ingredients of this medicine.
- you have or had severe mental disorders (such as depression or suicidal thoughts or if you tried to kill yourself).
- you have or had an autoimmune disease (such as rheumatoid arthritis, psoriasis or inflammatory bowel disease).
- you had an organ transplantation and you take medicines which suppress your immune system.
- you have advanced, uncontrolled liver disease.
- you have severe kidney disease.

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

- have or ever had any problems with your heart including heart attack or high blood pressure
- are being treated for a mental illness or had treatment in the past for any mental illness, including depression and have had thoughts of hurting yourself or others
- have thyroid disease
- have diabetes or high blood pressure. Your doctor may ask you to have an eye examination.
- have liver problems. You will have blood tests regularly to check how your liver is working if you are on long-term BESREMI® therapy.
- have or have had pancreas problems such as inflammation of the pancreas
- have kidney problems
- have a history of intestinal disorders such as colitis (inflammation of the colon)
- have lung (respiratory) problems, such as pneumonia, shortness of breath, and Chronic Obstructive Pulmonary Disease (COPD)
- have vision problems due to diseases such as diabetes or hypertension
- are pregnant or plan to become pregnant
- have psoriasis or other skin problems because they may get worse during treatment with BESREMI®

Other warnings you should know about:

- Dental and gum disorders, which may lead to loss of teeth, can occur with interferon medicines. In addition, dry mouth could damage teeth and the lining of the mouth during long-term treatment with BESREMI®. You should brush your teeth thoroughly twice daily and have regular dental checks.
- Reaching the optimal dose of BESREMI® may take time and can be different for different people. Your doctor will decide if it is necessary to treat you with another medicine for an early reduction of your blood cell number to prevent blood clots and bleeding.
- Give yourself time after taking BESREMI® to see how you feel before driving a vehicle or operating machinery.

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

Important safety information (continued)

Usual dose:

The usual starting dose of BESREMI[®] is 50 mcg or 100 mcg every 2 weeks. This depends on whether or not you were already taking other drugs to treat your disease. Your doctor will then increase your dose stepwise and may adjust your dose during treatment. Your dose will be increased gradually until your disease is under control or until you reach the maximum dose.

Overdose:

If you have taken more BESREMI[®] than you should, tell your doctor as soon as possible.

If you think you, or a person you are caring for, have taken too much BESREMI[®], contact a healthcare provider, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

You should inject the dose as soon as you remember. However, if more than 2 days have passed since you missed a dose, skip that dose and inject the next dose when it is due. Do not inject a double dose to make up for a forgotten dose. Check with your doctor or pharmacist if you are not sure what to do after missing a dose.

Possible side effects from using BESREMI[®]

These are not all the possible side effects you may have when taking BESREMI[®]. If you experience any side effects not listed here, tell your healthcare provider.

- decrease in the number of types of white blood cells (called leukocytes and neutrophils) that may increase your risk of infection, cause fever, chills or unusual fatigue, and in blood clotting cells (called platelets) which can result in bleeding if the number of cells drops too low
- feeling anxious, mood changes
- runny nose, sneezing, coughing, fever
- joint or muscle pain, back pain, bone pain
- increase or decrease in thyroid gland activity, increase of thyroid stimulating hormone leading to fatigue, weight gain or loss, rapid heartbeat, cold intolerance, dry skin
- tiredness, weakness, feeling very sleepy
- dry eyes
- headache
- loss of appetite
- dry mouth, constipation
- diarrhea, abdominal pain
- in blood tests, increases in certain liver enzymes
- itchy skin, hair loss, red skin, increased sweating, dry skin

Serious side effects and when to talk to your doctor

Talk to your doctor if you experience any of the following:

- Common:
 - Anxiety: feeling irritable, nervous or panic-stricken
 - Atrial fibrillation (when the heart beats very fast and uneven): chest discomfort with unpleasant awareness of your heartbeat, fatigue, weakness, dizziness, shortness of breath, feeling faint
 - Cataracts (clouding of the lens of the eye): blurry vision, seeing double, sensitivity to light or glare
 - Hypertension (high blood pressure): pounding in the ears, headache, blurred vision
 - Influenza like illness (flu-like symptoms) only if severe: headache, muscle aches, chills or a fever
 - Pancreatitis (severe and ongoing pain in the stomach area which could be a sign of inflamed pancreas)
 - Urinary tract infection (infection in urinary system including kidneys, ureters, bladder and urethra): frequent urination, pain or burning sensation while urinating, blood in the urine, pain in the pelvis, strong smelling urine, cloudy urine
- Uncommon:
 - Liver problems yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite, itching
- Unknown:
 - Endocrine disorders diabetes, increased thirst, frequent urination, unexplained weight loss, blurred vision, fatigue
 - Respiratory problems shortness of breath, fatigue, dizziness, chest pain, swelling of the ankles or legs

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 (canada.ca/drug-device-reporting) for information on how to report online, by mail, or by fax; or
- Calling toll-free at 1-866-234-2345.

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

What is BESREMI[®] used for?

BESREMI[®] is used to treat adults with a blood disorder called polycythemia vera.

Serious Warnings and Precautions

Interferons, including BESREMI[®], cause or aggravate fatal or life-threatening neuropsychiatric (mental illness), autoimmune (where the body's immune system attacks the body's own cells), ischemic (conditions in which blood flow, and thus oxygen, is restricted to a part of the body) and infectious disorders. If you have persistently severe or worsening signs or symptoms of these conditions you should contact your doctor. Your doctor will assess you and may discontinue you from therapy. In many cases, but not all cases, these disorders resolve after stopping interferon therapy.

Do not use BESREMI[®] if:

You are allergic to ropeginterferon alfa-2b or any of the other ingredients in BESREMI[®] or the container. You have or have had severe psychiatric disorders, particularly severe depression, suicidal thoughts, or a suicide attempt. You have decompensated cirrhosis of the liver. You have a history of or an active serious or untreated autoimmune disease. You are an immunosuppressed transplant recipient. You have thyroid disease unless it can be controlled with treatment. You have severe heart or blood vessel disease, such as uncontrolled high blood pressure, congestive heart failure, serious abnormal heart rhythm, significant narrowing of heart blood vessels, unstable angina, or recent stroke or heart attack. You have severe or end stage kidney disease.

These are not all the possible side effects you may have when taking BESREMI[®]. If you experience any side effects not listed here, tell your healthcare provider. If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

How to take BESREMI[®]

Use BESREMI[®] exactly as your healthcare provider tells you to. Your healthcare provider will tell you how much BESREMI[®] to inject and when to inject it. Do not inject more than your prescribed dose. Your healthcare provider should do blood tests before you start BESREMI[®], and regularly during treatment to monitor your polycythemia vera, and to check you for side effects.

For More Information

This brochure does not take the place of talking with your healthcare provider. For complete information about BESREMI[®], including Serious Warnings and Precautions, who should not use BESREMI[®], possible side effects, dosing, monitoring, and how to use BESREMI[®], please read the Patient Medication Information included with the BESREMI[®] package and speak with your healthcare professional. You can also visit www.besremipmi.ca or call FORUS Therapeutics Inc. at 1-866-542-7500.