PART III: CONSUMER INFORMATION

PrBETASERON®
Interferon beta-1b

This leaflet is part III of a three-part Product Monograph published when BETASERON was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about BETASERON. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
BETASERON (BAY-tah-SEER-on) is used for the treatment of relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations in ambulatory patients (ie, patients who are able to walk without help).

BETASERON is also used for the treatment of secondary-progressive multiple sclerosis to slow the progression of disability and to reduce the frequency of clinical exacerbations.

BETASERON is also approved for use in patients who have symptoms which are likely to be a first sign of multiple sclerosis (single clinical event suggestive of multiple sclerosis). Any other reasons which could explain the symptoms have to be ruled out. Your doctor will perform a test using an imaging machine (magnetic resonance imaging [MRI]). This test has to show at least two signs of inflammation in the central nervous system suggestive of multiple sclerosis.

What it does:
Multiple sclerosis is a life-long disease that affects your nervous system (ie, brain and spinal cord) by destroying the protective covering (myelin) that surrounds your nerve fibers. An abnormal response by the body's immune system is thought to play an important part in the process which damages the nervous system.

BETASERON is a form of protein called interferon beta that occurs naturally in the body. Interferon beta has been shown to modify the immune system response, but the exact way that BETASERON works in MS is unknown. BETASERON will not cure MS but it has been shown to decrease the number of flare-ups and slow the occurrence of some of the physical disabilities that are common in people with MS.

When it should not be used:
You should NOT use BETASERON:
- if you are pregnant; or
- if you have had previous allergic reactions, such as difficulty breathing, itching, flushing or hives, to interferon beta or to any of the nonmedicinal ingredients (see below).

What the medicinal ingredient is:
The active ingredient is interferon beta-1b.

What the nonmedicinal ingredients are:
BETASERON powder: human albumin, mannitol
Diluent: sodium chloride, water for injection

What dosage forms it comes in:
BETASERON is formulated as a sterile, white to off-white powder which must be dissolved using the supplied diluent. Each single-use vial contains 0.3 mg (9.6 million international units [MIU]) of interferon beta-1b. The diluent syringe contains 1.2 mL of sodium chloride 0.54% solution.

The prepared solution for injection contains 0.25 mg (8.0 MIU) of interferon beta-1b per 1 mL and is pH neutral.

WARNINGS AND PRECAUTIONS

BEFORE you use BETASERON, talk to your doctor if you have any of the following conditions:

- Depression, anxiety (feeling uneasy, nervous or fearful for no reason) or trouble sleeping
- Liver problems
- Epilepsy or a history of seizures
- Heart problems
- Problems with your thyroid gland
- Are breast-feeding or are planning to become pregnant

Allergic reactions: Some patients taking BETASERON have had severe allergic reactions leading to difficulty breathing and swallowing; these reactions can happen quickly. Allergic reactions can happen after your first dose or may not happen until after you have taken BETASERON many times. Less severe allergic reactions such as rash, itching, skin bumps, or swelling of the mouth or tongue can also happen. If you think you are having an allergic reaction, stop using BETASERON immediately and call your doctor.

Depression: Some patients treated with interferons, including BETASERON, have become seriously depressed (feeling sad). Some patients have thought about or have attempted to kill themselves. Depression (a sinking of spirits or sadness) is not uncommon in people with multiple sclerosis. However, if you are feeling noticeably sadder or helpless, or feel like hurting

yourself or others, you should tell a family member or friend right away and call your doctor or healthcare provider as soon as possible. Your doctor may ask that you stop using BETASERON. Before starting BETASERON, you should also tell your doctor if you have ever had any mental illness, including depression, and if you take any medications for depression.

Kidney problems: Blood clots in the small blood vessels may occur during your treatment. These blood clots could affect your kidney (thrombotic thrombocytopenic purpura or haemolytic uremic syndrome). This might happen several weeks to several years after starting BETASERON and may cause death. Talk to your doctor if you experience the following symptoms: increased bruising, bleeding, extreme weakness, headache, dizziness or light-headedness. Your doctor may want to check your blood pressure, blood (platelet count) and the function of your kidney.

Liver problems: BETASERON, like other interferon beta products, may cause severe liver problems. Some of the symptoms of liver problems are yellowing of the skin and whites of the eyes, malaise (a vague feeling of discomfort), fatigue, nausea, vomiting, abdominal pain, dark urine and itching of the skin. If you develop these symptoms while taking BETASERON, you should call your doctor right away.

Seizures: Some patients have had seizures while taking interferons. It is not known whether the seizures are related to the effects of MS, to interferons, or to a combination of both. If you have a seizure while taking BETASERON, you should call your doctor right away.

Heart problems: During treatment with BETASERON, cardiomyopathy (a disease of the heart muscle) has been reported in rare cases. If you experience symptoms like irregular heart beat, fluid retention (swelling) in the lower parts of your body (eg, ankles, legs), or shortness of breath, call your doctor immediately.

Thyroid problems: Some people taking BETASERON may develop changes in the function of their thyroid. Symptoms of these changes include feeling hot or cold much of the time or change in your weight (gain or loss) without a change in your diet or the amount of exercise you are getting.

Gastrointestinal problems: In rare cases, an inflammation of the pancreas has been observed with BETASERON use, often associated with an increase of triglycerides (a type of fat in the blood). If you have suffered from increased triglycerides or have had problems with your pancreas, please tell your doctor.

Risk to pregnancy: If you plan to become pregnant or could become pregnant while on BETASERON, advise your doctor. If you become pregnant while taking BETASERON you should stop using BETASERON immediately and call your doctor. BETASERON may cause you to lose your baby (miscarry) or may cause harm to your unborn child. You and your doctor will need to decide whether the potential benefit of taking BETASERON is greater than the potential risks to your unborn child. Should you become pregnant, please contact Bayer Medical Information at 1-800-265-7382.

Breast-feeding: You should talk to your doctor if you are breast-feeding an infant. It is not known if BETASERON can be passed to an infant in mother's milk, but because of the potential to cause a serious adverse reaction in an infant, a decision should be made whether to stop breast-feeding or stop taking BETASERON.

Immune system problems: The administration of interferons to patients with a pre-existing rare disturbance of the immune system where abnormal proteins are found in the blood (monoclonal gammopathy) has been associated with problems with small blood vessels leading to shock (collapse) and, in some cases, death.

Human albumin: This product contains a protein (albumin) extracted from human blood and so carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of a disease affecting the nervous system (Creutzfeld-Jakob disease) is also considered extremely remote.

Injection site problems: BETASERON may cause redness, pain or swelling at the place where an injection was given. A few patients have developed skin infections or areas of severe skin damage (necrosis). If one of your injection sites becomes swollen and painful or the area looks infected and it doesn't heal within a few days, you should call your doctor.

INTERACTIONS WITH THIS MEDICATION

With the exception of steroids or ACTH (anti-inflammatory medicines), the use of BETASERON together with other substances that modify the immune system response was not studied. Caution should be exercised when interferons are given in combination with other drugs which need a certain liver enzyme system (the cytochrome P450 system) for their metabolism. These drugs include some commonly used drugs against fever and pain.

You should tell your doctor if you are taking any other prescription or nonprescription medicines, including vitamin and mineral supplements and herbal products.

PROPER USE OF THIS MEDICATION

BETASERON is intended for use under the guidance and supervision of a physician. Your physician or his/her delegate should instruct you in the preparation and self-injection technique of BETASERON. Do not begin your BETASERON treatment without training.

Usual dose:
BETASERON should be used as prescribed by your doctor. The usual dose is 1 mL of prepared BETASERON solution injected subcutaneously (under the skin) every other day. This is equal to 0.25 mg (8 MIU).

If you have been prescribed BETASERON because you have symptoms likely to be a first sign of multiple sclerosis, your treatment should be started at a low dose of 0.25 mL (0.0625 mg or 2 MIU). Your dose will then be increased slowly until you reach a dose of 1 mL. Your individual tolerability of BETASERON will determine the rate of dose increase. Your doctor will decide this with you. To easily increase the dosage during the first 12 injections, you may be given a special Initiation Pack, containing four differently colored and numbered packs with specially marked syringes.

Your injections should be about 48 hours (two days) apart, so it is best to take them at the same time each day, preferably in the evening before bedtime.

Self-Injection Procedure

SAFETY TIPS

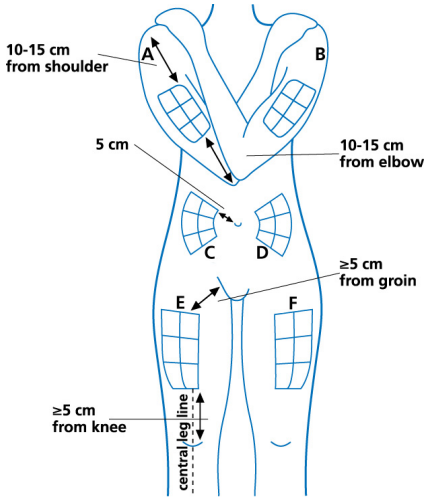
- Use only the supplies that come with your BETASERON package.
- Use only the diluent from the prefilled syringe.
- Wash your hands thoroughly with soap and water before starting.
- Keep the items sterile. Do not touch the needle, the piercing spike of the vial adapter, or the top of the cleaned vial.
- Make sure none of the items in your package have been opened or are damaged.
- Do not reuse opened materials. Throw away any unused portions of BETASERON and diluent.
- Throw away used syringes and needles in the proper disposal container.

STEP 1: CHOOSING AN INJECTION SITE

BETASERON should be injected into subcutaneous tissue (under the skin, between the fat layer and the muscles beneath). The best areas for injection are loose and soft, away from joints.

- Choose an injection site from the following areas (Figure 1):
  - A Right arm, upper back portion (at least 10-15 cm below the shoulder and 10-15 cm above the elbow)
  - B Left arm, upper back portion (at least 10-15 cm below the shoulder and 10-15 cm above the elbow)
  - C-D Abdomen, above the waistline (at least 5 cm on either side of the navel)
  - E Right thigh (at least 5 cm above the knee and 5 cm below the groin)
  - F Left thigh (at least 5 cm above the knee and 5 cm below the groin)
  - G Left buttock (upper, outer portion)
  - H Right buttock (upper, outer portion)
- Change injection areas every time you inject yourself. Give the site time to recover from the last injection. This will help prevent injection site reactions.
- Wait at least one week before reusing an area.
- Do not use any areas where you feel lumps, depressions, pain, or discoloration; talk to your doctor or nurse about anything you find.

Front



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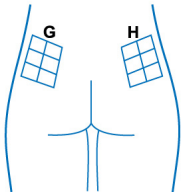

Figure 1

- Keep a record of when and where you are giving yourself injections. Use the BETASERON diary in your training kit.

STEP 2: CHECKING THE CONTENTS OF THE PACK[a]

If you have BETASERON in a single-use blister pack, please follow the blister pack instructions.
If you have BETASERON in a single-use carton, please follow the carton instructions.
If you have BETASERON in an Initiation Pack, please follow the Initiation Pack instructions.

BETASERON Blister Pack
Place the BETASERON single-use blister pack on a clean, flat surface in a well-lighted area. Ensure the pack contains:

- Vial of BETASERON
- Prefilled diluent syringe
- Three (3) alcohol wipes
- Vial adapter with attached 27-gauge, ½" needle in blister pack

BETASERON Carton
Place the BETASERON single-use carton on a clean, flat surface in a well-lighted area. Ensure the pack contains:

- Vial of BETASERON
- Prefilled diluent syringe
- Two (2) alcohol wipes
- Vial adapter with attached 30-gauge, ½" needle in blister pack

NOTE: *Please ensure you have a clean, dry cotton ball or gauze prior to preparing BETASERON for injection.*

BETASERON Initiation Pack
The Initiation Pack contains 4 differently colored and numbered triple packs for the first 12 injections. Ensure each triple pack you open contains:

- Three (3) vials of BETASERON
- Three (3) prefilled syringes
- Three (3) vial adapters with attached 30-gauge, ½" needle in blister pack
- Six (6) alcohol wipes

NOTE: *Please ensure you have a clean, dry cotton ball or gauze prior to preparing BETASERON for injection.*

Each triple pack contains the syringes you will require for preparing **each** dose. The syringes are specially marked accordingly with the appropriate doses (0.25, 0.50, 0.75, or 1.0 mL).

Start by using the **yellow pack** which is clearly marked with a **"1"** on the top right hand side of the box. This first pack should be used for treatment days 1, 3, and 5. It contains specially marked syringes with **0.25 mL** marking. This will help you to inject the required dose only.

After finishing with the yellow pack, start using the **red pack** which is clearly marked with a **"2"** on the top right hand side of the box. This second pack should be used for treatment days 7, 9, and 11. It contains specially marked syringes with **0.50 mL** marking. This will help you to inject the required dose only.

After finishing with the red pack, start using the **green pack** which is clearly marked with a **"3"** on the top right hand side of the box. This third pack should be used for treatment days 13, 15, and 17. It contains specially marked syringes with **0.75 mL** marking. This will help you to inject the required dose only.

Finally, after finishing with the green pack, start using the **blue pack** which is clearly marked with a **"4"** on the top right hand side of the box. This fourth pack should be used for treatment days 19, 21, and 23. It contains specially marked syringes with **0.25, 0.50, 0.75, and 1.0 mL** markings. This will help you to inject the required dose (1.0 mL) and familiarize you with the syringe used in the single-use packs.

STEP 3: INITIAL PREPARATION

1. Wash your hands thoroughly with soap and water.

2. Take out all the contents.
   NOTE: *Be sure the vial adapter blister pack is sealed and the rubber cap is firmly attached to the diluent syringe.*

3. Check the expiry date on the BETASERON vial and the prefilled diluent syringe.

4. Turn the single-use pack over, place the vial in the well (vial holder) in the center of the pack and place the prefilled diluent syringe in the U-shaped trough (if using a blister pack)

STEP 4: RECONSTITUTING BETASERON

1. **Remove** the BETASERON vial from the vial holder (if using a blister pack) and **take** the protective cap off the vial.

2. **Place** the vial back into the vial holder (if using a blister pack).

3. Use an alcohol wipe to **clean** the top of the vial. Move the wipe in one direction only. ***NOTE:*** *Leave the alcohol wipe on top of the vial until Step 4, point 5.*

[a] Not all presentations may be available in Canada.

4. **Peel** off the vial adapter blister pack label but do not remove the vial adapter. ***NOTE:*** *Be sure to avoid touching the vial adapter, in order to maintain its sterility.*

5. **Remove** the alcohol wipe on top of the BETASERON vial. **Place** the vial adapter (still in the blister packaging) on top of the BETASERON vial by pushing it until it pierces the rubber top of the BETASERON vial and snaps in place (Figure 2). Remove the blister packaging from the vial adapter.

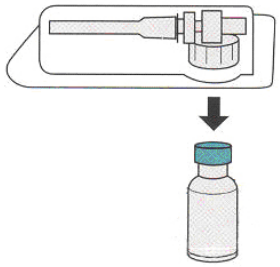

Figure 2

6. **Remove** the rubber cap from the diluent syringe with a twist and pull motion. Discard the rubber cap.

7. **Connect** the syringe with the vial adapter by turning clockwise and tighten carefully. This will form the syringe assembly (Figure 3).

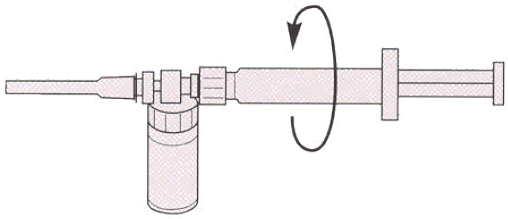

Figure 3

8. It is important to **slowly push** the plunger of the diluent syringe all the way in, keeping the syringe assembly at an angle. This will transfer all of the diluent drop by drop into the BETASERON vial (Figure 4).

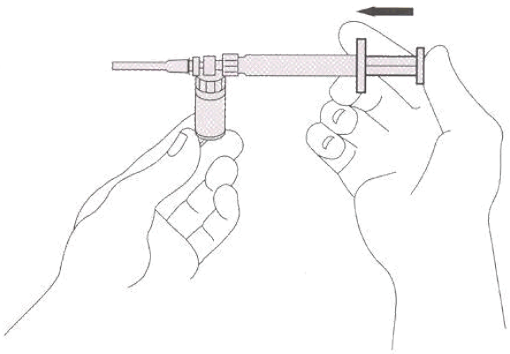

Figure 4

9. Keeping the plunger depressed, with the syringe assembly attached, **swirl** the vial **gently** to completely dissolve the white cake of BETASERON. **(DO NOT SHAKE.)**

10. **Look** closely at the BETASERON solution for particles. It should be clear. **NOTE:** *If the mixture contains particles or is discolored, discard it and start again. Foaming may occur during reconstitution, or if it is swirled or shaken too vigorously. If so, allow the vial to sit undisturbed until the foam settles.*

STEP 5: PREPARING THE INJECTION

1. Keeping the plunger depressed, turn the assembly upside down (ie, 180 degrees) so that the vial is on top. The syringe remains horizontal (Figure 5).

2. **BETASERON Single-use blister or carton:**
   Slowly **pull** the plunger back to withdraw the entire contents of the BETASERON vial into the syringe (Figure 5).
   NOTE: *If 1 mL of clear solution cannot be withdrawn from the vial, discard the vial and syringe and start over.*

   BETASERON Initiation Pack:
   With the Initiation Pack, withdraw the solution from the BETASERON vial **only up to the mark on the syringe**:
   - 0.25 mL for the first three injections (on day 1, 3, and 5 of therapy); or
   - 0.5 mL for the injections on day 7, 9, and 11 of therapy; or
   - 0.75 mL for the injecions on day 13, 15, and 17 of therapy.

   Discard the vial with any remaining solution.

   From day 19 onwards, you are injecting the **full dose 1.0 mL**.

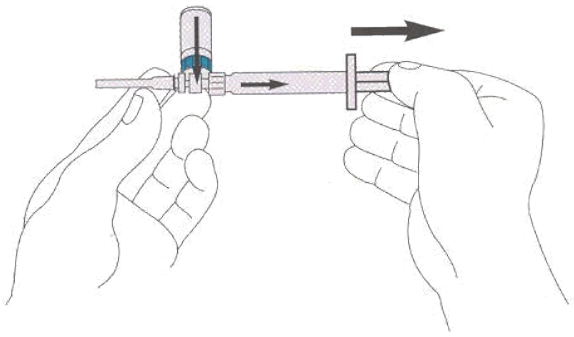

Figure 5

3. **Turn** the syringe assembly so that the needle end is pointing up. Tap the syringe gently so any air bubbles will rise to the top. Tap the syringe with the side of your finger. Do not tap the syringe with a hard object because the glass syringe could break. Push the plunger to the 1 mL mark (or to the amount prescribed by your doctor) to remove any air bubbles.

   If you are injecting less than 1.0 mL with the Initiation Pack, there might not be any air bubbles; however, for the full dose injection, some air bubbles might be seen. Remove them by gently tapping the syringe and pushing the plunger to the respective marking on the syringe.

   NOTE: *If too much solution is expelled into the vial, repeat Step 5, points 1, 2, and 3.*

4. **Remove** the vial adapter and the vial from the syringe by grasping the plastic cap of the vial adapter and twisting it clockwise, as shown in Figure 6. This will release the vial adapter, with the vial, from the syringe but leave the needle on the syringe (Figure 6).

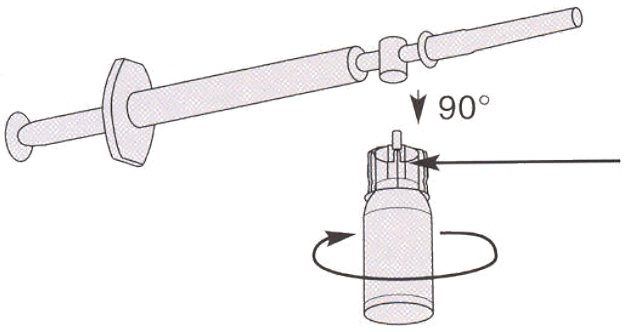

Figure 6

5. **You have now reconstituted your BETASERON and are ready to be injected.**

The injection should be administered immediately after mixing. If you are unable to give the injection immediately, you may refrigerate the medication in the syringe and inject within three hours. Do not freeze.

STEP 6: INJECTING BETASERON

Optional - Autoinjector: If you have been given an autoinjector, you should follow the detailed instructions that are supplied with it.

- **The Single-use blister pack can only be used with the BETAJECT® III autoinjector.**
- **The Single-use carton can only be used with the BETAJECT® Lite, BETACOMFORT® or BETACONNECT® autoinjector.**
- **The Initiation Pack can only be used with the BETAJECT® Lite, BETACOMFORT® or BETACONNECT® autoinjector.**

1. Use a fresh alcohol wipe to **clean** the skin at the injection site. Use a circular motion from the center of the injection site outward. Let the alcohol dry.
2. **Throw away** the wipe.
3. **Remove** the protective needle guard from the needle by pulling it without turning.
4. Gently **pinch** the skin around the site to lift it up a bit.
5. **Stick** the needle straight into the skin at a 90° angle with a quick, firm motion.
6. **Inject** the drug by using a slow, steady push (push the plunger all the way in until the syringe is empty).
7. **Remove** the needle from the skin.
8. Gently **massage** the injection site with a clean, dry cotton ball or gauze (or as directed by your healthcare professional).
9. **Throw away** the syringe in the disposal unit.
10. **Discard** all other components.

Overdose:
If you accidentally take more than your prescribed dose, or take it two days in a row, call your doctor right away.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Center immediately, even if there are no symptoms.

Missed Dose:
If you miss a dose, you should take your next dose as soon as you remember or are able to take it. Your next injection should be given about 48 hours (two days) after that dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with any prescription medication, side effects related to therapy can occur. Consult your doctor if you have any problems, whether or not you think they may be related to BETASERON.

Skin reactions: Injection site reactions are common. They include redness, pain, swelling and discoloration. Less frequently, injection site necrosis (skin breakdown and tissue destruction) has been observed. To minimize the chance of a reaction, change injection areas every time you inject yourself and wait at least one week before reusing an area. Do not inject into skin that is tender, red, or hard. Do not use any areas where you feel lumps, depressions, pain, or discoloration. Injection site reactions may occur less frequently if you use an autoinjector. Talk to your doctor or nurse about anything you find. If you experience a break in the skin or drainage of fluid from the injection site, consult your doctor. The occurrence of injection site reactions decreases over time.

Flu-like symptoms: Flu-like symptoms are also common. They include fever, chills, sweating, fatigue, and muscle aches. For many patients, these symptoms will lessen or go away over time. Taking BETASERON at night may help lessen the impact of flu-like symptoms. You should talk to your doctor about whether you should take an over-the-counter medicine for pain or fever reduction (nonsteroidal anti-inflammatory drugs [NSAIDs] or acetaminophen) before or after taking your dose of BETASERON.

Liver problems: Your liver function may be affected. Elevations of liver function values occurred very commonly in patients treated with BETASERON in clinical studies and in most cases were mild and transient. Rare cases of severe liver injury have been reported (see **WARNINGS AND PRECAUTIONS – Hepatic/Biliary/Pancreas**).

Blood problems: A decrease of infection-fighting white blood cells, red blood cells, or platelets (cells that help you form blood clots) may occur. If decreases are severe, they can lessen your ability to fight infections, make you feel tired or sluggish or cause you to bruise or bleed easily.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / Effect		Talk with your doctor or pharmacist		Stop taking drug and seek emergency medical treatment
		Only if severe	In all cases	
Very common	Rash		✓	
Common	Break in skin or drainage of fluid at injection site		✓	
	Lack of coordination in moving arms, fingers or legs, or other muscular movement		✓	
Uncommon	Difficulty breathing or swallowing, swelling of mouth or tongue			✓
	Depression or suicidal thoughts		✓	
	Fluid retention (swelling) in ankles or legs		✓	
	Seizures		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / Effect		Talk with your doctor or pharmacist		Stop taking drug and seek emergency medical treatment
		Only if severe	In all cases	
	Symptoms of liver problems: yellowing of the skin and whites of eyes, malaise, fatigue, nausea, vomiting, abdominal pain, dark urine, itching of the skin		✓	
	Symptoms of kidney problems: foamy urine, fatigue, swelling, particularly in the ankles and eyelids, and weight gain		✓	

This is not a complete list of side effects. For any unexpected effects while taking BETASERON, contact your doctor or pharmacist.

HOW TO STORE IT

Before reconstitution: Store BETASERON between 2°C to 25°C. Excursions between 25°C and 30°C are permitted as long as they do not exceed a maximum of 30 days. Do not freeze.

After reconstitution: If not used immediately, reconstituted BETASERON must be refrigerated and used within three hours. Do not freeze.

Keep syringes and needles away from children. Do not reuse needles or syringes. Discard used syringes and needles in a syringe disposal unit.

REPORTING SUSPECTED SIDE EFFECTS

Canada Vigilance Program:

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

Report online at www.healthcanada.gc.ca/medeffect
Call toll-free at 1-866-234-2345
Complete a Canada Vigilance Reporting Form and:

- Fax toll-free to 1-866-678-6789, or
- Mail to: Canada Vigilance Program
  Health Canada
  Postal Locator 0701E
  Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect

Note: Should you require information related to the management of side effects, please contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your health professional or pharmacist first, or Bayer Medical Information at 1-800-265-7382 or canada.medinfo@bayer.com.

This document plus the full Product Monograph, prepared for health professionals can be found at: http://www.bayer.ca or by contacting the manufacturer at the above-mentioned phone number and email address.

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