

PART III: CONSUMER INFORMATION

 **VICTRELIS TRIPLE™**

VICTRELIS™
boceprevir

PLUS

PEGETRON®
ribavirin
plus
peginterferon alfa-2b

This leaflet is part III of a three-part “Product Monograph” published when VICTRELIS TRIPLE™ was approved for sale in Canada and is designed specifically for Consumers. Please read this information carefully before starting your VICTRELIS TRIPLE™ therapy. It is important to read this each time your prescription is refilled in case new information becomes available. This leaflet is a summary and will not tell you everything about VICTRELIS TRIPLE™. Contact your doctor or pharmacist if you have any questions about the drug.

You should talk with him or her before starting therapy and at your regular check-ups. This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

ABOUT THIS MEDICATION

What the medication is used for:

VICTRELIS TRIPLE™ is a prescription medicine used to treat chronic (lasting a long time) hepatitis C genotype 1 infection in adults who have not been previously treated or who have failed previous therapy. Patients with hepatitis C have the virus in their blood and in their liver.

It is not known if VICTRELIS TRIPLE™ is safe and effective when used in children (< 18 years of age).

What it does:

VICTRELIS TRIPLE™ therapy consists of 3 active medications in 2 drug products: VICTRELIS™ (boceprevir) and PEGETRON®, (ribavirin and peginterferon alfa-2b).

Boceprevir is a medicine called a Hepatitis C Virus Protease Inhibitor that directly targets Hepatitis C Virus to reduce the amount of virus in your body.

Ribavirin is an antiviral agent (fights infection), but does not work when used by itself to treat chronic hepatitis C.

Peginterferon alfa-2b generally helps the body's immune system to fight infections.

It is not known exactly how ribavirin and peginterferon alfa-2b work together to fight the hepatitis C infection.

VICTRELIS TRIPLE™ therapy may reduce the amount of hepatitis C virus in the blood stream to below the level that can be measured by a laboratory test.

When it should not be used:

Do not use VICTRELIS TRIPLE™:

- **If you or your partner are pregnant.**
- **If you or your partner plan to become pregnant during treatment or during the 6 months after treatment.**
- **If you or your partner become pregnant during treatment.** VICTRELIS TRIPLE™ therapy can cause serious birth defects or harm to your unborn child. Therefore, both you and your partner **must use effective contraception** during this time.
- If you are allergic to any of the ingredients in VICTRELIS TRIPLE™ (boceprevir, ribavirin or peginterferon alfa-2b) or to any of the excipients (see **What the non-medicinal ingredients are**).
- If you have autoimmune hepatitis (hepatitis caused by cells in your body attacking each other) or any other problem with your immune system; if you are taking medicine that suppresses your immune system (your immune system protects you against infection and some diseases).
- If you have a severe nervous or mental disorder.
- If you have thyroid disease that is not well controlled with medicines.

- If you have advanced uncontrolled liver disease (other than hepatitis C).
- If you have severe kidney disease.
- If you have epilepsy.
- If you are breastfeeding.
- If you are taking certain medicines. For more information about medicines that you should not take while using VICTRELIS TRIPLE™, please see **INTERACTIONS WITH THIS MEDICATION**.

What the medicinal ingredients are:

- boceprevir capsules
- ribavirin capsules
- peginterferon alfa-2b powder for solution

What the non-medicinal ingredients are:

Boceprevir capsules: Non-medicinal ingredients are croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pre-gelatinized starch, and sodium lauryl sulfate. The capsule shell consists of gelatin, red iron oxide, titanium dioxide, and yellow iron oxide. The capsule is printed with red ink. The red ink contains red iron oxide and shellac.

Ribavirin capsules: Non-medicinal ingredients are croscarmellose sodium, lactose monohydrate, magnesium stearate and microcrystalline cellulose. The capsule shell contains gelatin, sodium lauryl sulfate, silicon dioxide, and titanium dioxide.

Peginterferon alfa-2b Powder for Solution in REDIPEN® single dose delivery system: Non-medicinal ingredients are polysorbate 80, sodium phosphate dibasic anhydrous, sodium phosphate monobasic dihydrate, and sucrose.

What dosage forms it comes in:

Each boceprevir capsule contains 200 mg of boceprevir.

Each ribavirin capsule contains 200 mg of ribavirin.

Peginterferon alfa-2b REDIPEN® single dose delivery system consists of a dual-chamber glass cartridge with a chamber containing peginterferon alfa-2b as a white to off-white lyophilized powder and another chamber containing Sterile Water for Injection. The cartridge is provided in a pen device for reconstitution, dose preparation and subcutaneous administration. It is available in strengths of 80, 100, 120, and 150 mcg for single use.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Some people get depressed when taking pegylated interferon alfa-2b alone or in combination treatment with ribavirin, and in some cases people had thoughts about threatening the life of others, suicidal thoughts or aggressive behaviour (sometimes directed against others). Some patients have actually committed suicide. Be sure to seek emergency care if you notice that you are becoming depressed or have suicidal thoughts or change in your behaviour. You may want to consider asking a family member or close friend to help you stay alert to signs of depression or changes in your behaviour.

What is the most important information I should know about VICTRELIS TRIPLE™ therapy?

1. **VICTRELIS TRIPLE™ therapy could cause serious birth defects or harm your unborn child.**
 - **If you or your partner are pregnant, you should not receive VICTRELIS TRIPLE™.**
 - **Pregnancy should not be planned while you or your partner are on therapy or for 6 months after therapy.**
 - **If you or your partner become pregnant while on therapy or during the 6 months after stopping therapy, consult your doctor immediately.** Your doctor should call the Merck Canada Inc. Medical Information Department at 1-800-567-2594.
 - **If you are a woman of childbearing age, you must have a negative pregnancy test before treatment and a pregnancy test each month during treatment.**
 - **Both you and your partner must use effective contraception during treatment and for the 6 months after treatment is completed.** As systemic (e.g., oral, topical...) hormonal contraceptives may not work as well while taking VICTRELIS TRIPLE™, use of 2 alternative methods of contraception, such as barrier method and intrauterine devices during treatment with VICTRELIS™ and ribavirin. **You should discuss with your doctor how you or your partner can prevent getting pregnant.**
2. **Ribavirin may cause anemia, which is a decrease in the number of red blood cells you have. Anemia may be increased when boceprevir is added to peginterferon alpha/ribavirin therapy. This can be dangerous, especially for patients who already have heart**

or circulatory (cardiovascular) problems. Talk with your doctor before taking VICTRELIS TRIPLE™ therapy if you have or have ever had any cardiovascular problems. Your healthcare provider will be checking your blood counts periodically for possible decreases in your blood count. Depending on the medications that you are taking, your healthcare provider may make changes to your current medicines or prescribe additional medicines to treat your anemia.

3. **Boceprevir may cause serious side effects when taken with other medications. It is important to know the medicines that should not be taken with boceprevir.**
4. **Do not take boceprevir alone to treat chronic hepatitis C infection. Boceprevir should only be used with other medicines to treat chronic hepatitis C infection.**

Medicines are sometimes prescribed for purposes other than those listed in this package leaflet. Remember, this medicine is for you and must be used as prescribed by your doctor. Never give it to anyone else.

BEFORE you use VICTRELIS TRIPLE™ talk to your doctor or pharmacist if you have any of the following medical conditions or other serious medical problems:

- Previous heart attack, or other heart problems, because therapy may cause heart problems to become worse.
- Blood disorders; including anemia (low red blood cell count), thalassemia (Mediterranean anemia), sickle-cell anemia, and neutropenia (low neutrophil count) because therapy may further reduce the number of red and white blood cells you have. This may make you feel dizzy or weak and could worsen any heart problems you might have.
- Kidney problems.
- Liver problems (except hepatitis C infection).
- Nervous or mental problems (such as depression, anxiety, etc.), because the therapy could make these problems worse.
- Body organ transplant and are taking medicine that keeps your body from rejecting your transplant (suppresses your immune system).

- Thyroid disease.
- Cancer.
- Infection with hepatitis B virus and/or Human Immunodeficiency Virus (the virus that causes AIDS).
- If you have had problems with your immune system.
- If you have diabetes or high blood pressure, your doctor may ask you to have periodic eye examinations.
- If you have high blood fat levels (such as elevated triglycerides or cholesterol levels).
- If you had any serious illness affecting your breathing or your blood.
- If you have psoriasis or sarcoidosis, it may become worse while you are using VICTRELIS TRIPLE™.
- If you have any other medical condition.
- Be sure to tell your doctor about all the medications you are taking, including those without a prescription, and the Chinese herbal medication Shosaikoto (also known as Xiao-Chai-Hu-Tang).
- If you are using any other medications.

VICTRELIS TRIPLE™ may cause a Reduction of Red Blood Cells a condition known as anemia, or a reduction of neutrophils (a type of white blood cell) a condition known as neutropenia. Anemia or neutropenia may be increased when VICTRELIS™ is added to your ribavirin therapy. Therefore, your healthcare provider will be checking your blood counts periodically for possible decreases in your blood cell counts. Depending on the medications that you are taking, your healthcare provider may make changes to your current medicines or prescribe additional medicines to treat your anemia, or neutropenia.

VICTRELIS TRIPLE™ may cause serious side effects when taken with other medications. It is important to know the medicines that should not be taken with VICTRELIS™.

Dental and gum disorders, which may lead to loss of teeth, have been reported in patients who received VICTRELIS TRIPLE™. In addition, dry mouth could have a damaging effect on teeth and membranes of the mouth during long-term treatment with VICTRELIS TRIPLE™. You should brush your teeth thoroughly twice daily and have regular dental examinations. In addition some patients may experience vomiting. If you have this reaction, be sure to rinse your mouth thoroughly afterwards.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with ribavirin and/or peginterferon alfa-2b include: medications metabolized by CYP1A2, CYP2C8/9 and CYP2D6; reverse transcriptase inhibitors such as zidovudine and stavudine; purine nucleoside analogues such as didanosine and abacavir; and Highly Active Anti-Retroviral Therapy.

Co-administration of ribavirin capsules and didanosine is not recommended due to the risk of lactic acidosis (a build-up of lactic acid in the body) and pancreatitis.

Tell your doctor or pharmacist if you are taking SEBIVO* (telbivudine) for chronic hepatitis B because taking this medicine together with pegylated interferon alfa-2b may increase your risk of developing peripheral neuropathy (numbness, weakness, tingling, and/or burning sensations, or pain in the arms and/or legs). The combined use of these medications is not recommended.

Do not take VICTRELIS TRIPLE™ if you take:

- alfuzosin – used to treat enlarged prostate;
- amiodarone, propafenone and quinidine – used for heart beat problems;
- astemizole¹, terfenadine¹ – used to treat allergies, hives, itching and watery eyes;
- birth control pills that contain drospirenone;
- carbamazepine, phenobarbital, phenytoin – used to treat seizures and nerve pain;
- cisapride¹ – used to help with digestion;
- ergot-containing medicines used to treat migraines, such as:
 - ergotamine,
 - dihydroergotamine,
 - ergonovine,
 - methylergonovine;
- lovastatin, simvastatin – used for lowering high cholesterol and triglycerides;
- oral midazolam, oral triazolam – used to help you sleep;
- pimozone – used for mental health problems;

¹ Please note that cisapride, astemizole and terfenadine are no longer available on the Canadian market.

- rifampin – used to treat tuberculosis or meningitis;
- sildenafil and tadalafil – used for the treatment of pulmonary arterial hypertension;
- St. John's Wort (*Hypericum perforatum*) – an herbal product used to help with your mood.

Tell your doctor if you are taking any of the following medications as they may interact with boceprevir. The dosage of one or the other may have to be changed or the medication avoided:

- atorvastatin, bepridil, bosentan, budesonide, buprenorphine, colchicine, cyclosporine, desipramine, dexamethasone, digoxin, felodipine, fluticasone, fluvastatin, methadone, nicardipine, nifedipine, pravastatin, rifabutin, rosuvastatin, salmeterol, sirolimus, tacrolimus, trazodone, and warfarin.

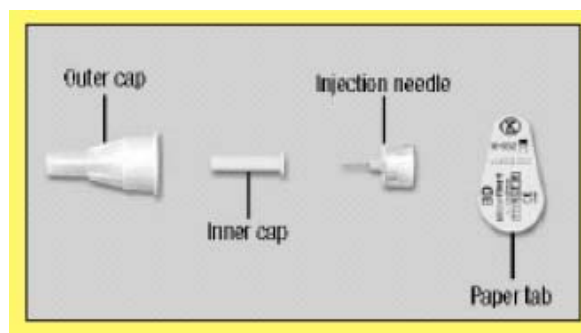
PROPER USE OF THIS MEDICATION

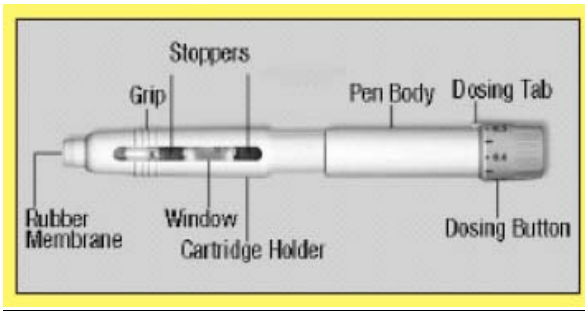
- Take VICTRELIS TRIPLE™ exactly as your healthcare provider tells you. Your healthcare provider will tell you how much to take and when to take it.
- Tell your doctor, pharmacist or health professional if you notice any change in the appearance of boceprevir capsule, ribavirin capsule or peginterferon alfa-2a powder for solution.
- Always take VICTRELIS™ and ribavirin with food.

The following instructions explain how to reconstitute and inject peginterferon alfa-2b powder for solution yourself. Please read the instructions carefully and follow them step by step. Your doctor or his/her assistant will instruct you how to self-inject peginterferon alfa-2b. Do not attempt to inject yourself unless you are sure you understand the procedure and requirement of self-injection.

Carefully follow the instructions provided.

How to use the peginterferon alfa-2b REDIPEN®





The following instructions explain how to inject yourself with the single use peginterferon alfa-2b REDIPEN®. **Please read the instructions carefully and completely before attempting to use the pen and follow them step by step.** Your doctor or his/her assistant will instruct you on how to self-inject with the peginterferon alfa-2b REDIPEN®. Do not attempt to inject yourself unless you are sure you understand the procedure and requirements for self-injection.

The peginterferon alfa-2b REDIPEN® is intended for use by one person only and must not be shared. Use the injection needle and alcohol swabs provided in the packaging only for the peginterferon alfa-2b REDIPEN®. Be sure the solution is at room temperature at the time of injection. Your doctor will have told you what dose you require for your therapy.

Note: The color of the dosing button is different for each strength of the peginterferon alfa-2b REDIPEN®.

Step 1: Mixing

It is important that you keep the peginterferon alfa-2b REDIPEN® upright (as shown in Figure 1) during mixing, unless otherwise instructed.

- Take the peginterferon alfa-2b REDIPEN® out of the refrigerator. Allow the medicine to come to room temperature.
- Wash your hands with soap and water.
- **Place the peginterferon alfa-2b REDIPEN® upright in the holder of the tray provided in the pack (the dosing button will be on the bottom) (Figure 1).**



Figure 1

- You may want to hold the REDIPEN® using the grip. To mix the powder and the liquid, press the two halves together firmly by pressing down until you hear the REDIPEN® click. The two stoppers should come together.
- Wait for several seconds until the powder is completely dissolved.
- **Gently turn the peginterferon alfa-2b REDIPEN® upside down twice. To avoid excessive foaming, do not shake.**
- Maintaining the peginterferon alfa-2b REDIPEN® upright, check the mixed peginterferon alfa-2b solution through the window. If there is still foam, wait until it settles. The solution should be clear and colorless. **Do not use the pen if the solution is discolored or irregular or contains any particles.**
- Keeping the peginterferon alfa-2b REDIPEN® upright in the holder provided in the packaging, disinfect the rubber membrane of the peginterferon alfa-2b REDIPEN® with one alcohol swab.
- Take the injection needle provided in the tray and remove its protective paper tab.
- **Maintaining the peginterferon alfa-2b REDIPEN® upright in the holder,** gently push the injection needle onto the REDIPEN® and **screw it securely in place (Figure 2).**



Figure 2

Keep the peginterferon alfa-2b REDIPEN® pointed up.

- **Do not take off the outer needle cap at this point.**
- You may see some liquid trickle out from under the cap, as the air has been expelled out of the pen.
- Wait about 5 seconds for this process to finish.
- **Check through the window to be sure that the two stoppers are together. If they are not together, do not use this pen because you may not be able to dial your dose (Figure 3).**

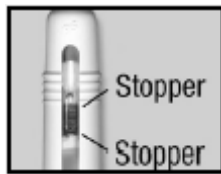


Figure 3

Step 2: Setting the dose

- Remove the peginterferon alfa-2b REDIPEN[®] from the holder.
- Holding the peginterferon alfa-2b REDIPEN[®] firmly, pull the dosing button out as far as it will go, until you see a **dark ring** on the pen. The dosing button should be easy to pull out without excessive force being required (Figure 4).



Figure 4

Note: Do not push the dosing button back in at this time. You will push it in when you are ready to self-inject the peginterferon alfa-2b.

- Turn the dosing button until your prescribed dose is aligned with the dosing tab. The button should turn easily without excessive force being required (Figure 5).



Figure 5

Note: If you cannot easily pull out the dosing button or dial the dose, do not use excessive force and do not use this pen because it may not deliver the correct dose.

Step 3: Injecting the solution

- Select the injection site. Your doctor will have told you which sites to use (e.g., thigh or abdomen).

Note: Change your injection site each time.

- Clean the injection site skin with the second alcohol swab.
- Pull off the **outer needle cap** (Figure 6).

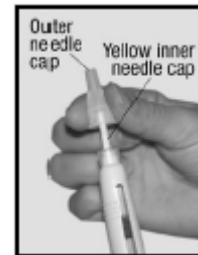


Figure 6

- There may be some liquid around the inner needle cap. This liquid is not part of your dose, this is extra. This is normal, as the air has been expelled out of the needle.
- Once the injection site is dry, pull off the **yellow inner needle cap** carefully exposing the injection needle.
- Hold the peginterferon alfa-2b REDIPEN[®] with your fingers wrapped around the pen body and your thumb on the dosing button (Figure 7).



Figure 7

- With your other hand, pinch a fold of loose skin.
- Insert the needle into the pinched skin at an angle of 45° to 90°.
- Press the dosing button down **slowly** and **firmly** until the button can no longer move.
- **Maintain pressure on the dosing button for an additional 5 seconds** to ensure that you get the complete dose.

- Remove the needle from your skin.
- Press the injection site with a small bandage or sterile gauze if necessary for a few seconds.
- Do not massage the injection site. If there is bleeding, cover with an adhesive bandage.
- Discard the peginterferon alfa-2b REDIPEN® with the needle safely in a closed rigid container.

Usual Adult Dose:

Your doctor has determined the correct dose of ribavirin and peginterferon alfa-2b based on your weight and the regimen (plan of treatment) that you are following for hepatitis C. Boceprevir 800 mg Three Times Daily will be used in combination with peginterferon alpha and ribavirin. Boceprevir will only be added to the treatment from the start of the fifth week. The total duration of your treatment will depend on the way in which your virus responds to treatment.

Your doctor may adjust your dose and length of time you take this treatment according to your response. Blood tests will be done regularly to help your doctor to know if it is working and if the dose needs to be changed.

If you have or develop severe kidney or liver problems, this treatment will be stopped. This treatment is not recommended for use in patients under the age of 18 years.

Based on the results of a clinical trial, the recommended dose of peginterferon alfa-2b is 1.5 mcg/kg/week in combination with ribavirin, which are dosed by patient weight. Peginterferon alfa-2b should be administered as subcutaneous injection once a week.

Ribavirin capsules are taken daily. Ribavirin capsules are to be administered orally, 800–1,400 mg, each day in two divided doses with food (morning and evening).

PATIENTS WHO HAVE NEVER BEEN TREATED

Recommended Dose

peginterferon alfa-2b: 1.5 mcg/kg/week

ribavirin: 800–1,400 mg daily based upon patient weight

boceprevir: 800 mg (four 200 mg capsules) three times daily (every 7 to 9 hours)

Dosing Recommendations^a

Patient Weight (kg)	peginterferon alfa-2b Powder for Solution		ribavirin Capsules	
	Weekly Dose (mcg/kg)	REDIPEN® Size (mcg/0.5 mL) ^b	Daily Dose (mg)	Number of Capsules (200 mg)
40 to 50	1.5	80	800	2 x 200 mg capsules A.M. 2 x 200 mg capsules P.M.
51 to 65	1.5	100	800	2 x 200 mg capsules A.M. 2 x 200 mg capsules P.M.
66 to 80	1.5	120	1,000	2 x 200 mg capsules A.M. 3 x 200 mg capsules P.M.
81 to 105	1.5	150	1,200	3 x 200 mg capsules A.M. 3 x 200 mg capsules P.M.
> 105	1.5	c	1,400	3 x 200 mg capsules A.M. 4 x 200 mg capsules P.M.

- The daily dose for ribavirin approximately falls within 13 ± 2 mg/kg/day.
- When reconstituted as instructed
- Should be calculated based on the body weight of an individual patient

PATIENTS WHO FAILED PRIOR TREATMENT

Recommended Dose

Peginterferon alfa-2b: 1.5 mcg/kg/week

Ribavirin: 800–1,400 mg daily based upon patient weight

boceprevir: 800 mg (four 200 mg capsules) three times daily (every 7 to 9 hours)

Dosing Recommendations^a

Patient Weight (kg)	peginterferon alfa-2b Powder for Solution		ribavirin Capsules	
	Weekly Dose (mcg/kg)	REDIPEN® Size (mcg/0.5 mL) ^b	Daily Dose (mg)	Number of Capsules (200 mg)
40 to 50	1.5	80	800	2 x 200 mg capsules A.M. 2 x 200 mg capsules P.M.
51 to 65	1.5	100	800	2 x 200 mg capsules A.M. 2 x 200 mg capsules P.M.
66 to 85	1.5	120	1,000	2 x 200 mg capsules A.M. 3 x 200 mg capsules P.M.
86 to 105	1.5	150	1,200	3 x 200 mg capsules A.M. 3 x 200 mg capsules P.M.
> 105	1.5	c	1,400	3 x 200 mg capsules A.M. 4 x 200 mg capsules P.M.

- The daily dose for ribavirin approximately falls within 13 ± 2 mg/kg/day.
- When reconstituted as instructed
- Should be calculated based on the body weight of an individual patient

It is important to follow your dosing schedule and your doctor's instructions on how to take your medications. Take the medicine for as long as prescribed and do not exceed the recommended dosage.

Always take boceprevir with food (a meal or a light snack, such as a piece of fruit or crackers).

Take the ribavirin capsules by mouth with water and during your meal. Do not chew the capsules.

Peginterferon alfa-2b is given at a dose of 1.5 mcg/kg once a week. Peginterferon alfa-2b is for subcutaneous use. This means that it is injected through a short injection needle into the fatty tissue just under your skin. If you are injecting this medicine yourself, you will be instructed how to prepare and give the injection.

If you are injecting peginterferon alfa-2b yourself, please be sure that the dose that has been prescribed for you is clearly provided on the package of medicine you receive. Inject peginterferon alfa-2b on the same day each week. Injecting it at the same time of day each week will help you not to forget to take it. Take the dose as soon as you remember, then continue your treatment as usual. Do not take a double dose to make up for forgotten individual doses. Contact your doctor or pharmacist if needed.

Overdose:

The primary effects of overdose were an increased incidence and severity of adverse events reported at the therapeutic doses of VICTRELIS TRIPLE™.

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

Missed Dose:

If you miss a dose of boceprevir and it is less than 2 hours before the next dose is due, the missed dose should be skipped. If you miss a dose and it is more than 2 hours before the next dose is due, take the missed dose with food and continue the normal dosing schedule. Do not double the next dose. If you have questions about what to do, call your healthcare provider.

If you miss a dose of ribavirin, take the missed dose as soon as possible during the same day. If an entire day has gone by, check with your doctor about what to do. Do not double the next dose.

If you miss a dose of peginterferon alfa-2b, take the missed dose as soon as possible during the same day or on the next day, and continue the dosing schedule provided to you by your doctor. If several days go by, check with your doctor about what to do. Do not double the next dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

What are the possible side effects of VICTRELIS TRIPLE™ therapy?

Like all medicines, VICTRELIS TRIPLE™ can have side effects. Although not all of these side effects may occur, they may need medical attention if they do occur.

VICTRELIS TRIPLE™ may cause serious side effects, including:

- Blood problems. Boceprevir can cause low red cell counts (anemia) or low neutrophil (neutropenia), which is a type of white blood cell, and low platelet counts (thrombocytopenia). In some people, these blood counts may fall to dangerously low levels.

Check with your doctor immediately if any of the following side effects occur during treatment:

- chest pain or persistent cough;
- symptoms of a severe allergic reaction (such as difficulty breathing, wheezing, or hives);
- symptoms associated with a cold or other respiratory infection, such as difficulty breathing or cough;
- shortness of breath;
- fever or chills beginning after a few weeks of treatment;
- changes in the way your heart beats;
- feeling depressed or hopeless, or thinking about death (suicidal thoughts or attempts);
- confusion, aggressiveness (sometimes directed against others), hallucination;
- trouble sleeping;
- severe stomach pain, black or tar-like stools, blood in stool or urine, feelings of numbness or tingling;
- severe bleeding from your nose;
- lower back or side pain, painful or difficult urination;
- problems with your eyesight or hearing;
- you notice that you are unusually tired and pale, and bruise easily.

Other events that may occur with this treatment are:

- irritation or pain at the site of injection;
- general discomfort, such as headache, fatigue or sleepiness, chills, fever, “flu-like” symptoms, weakness, pain around the ribs on the right side, feeling generally unwell, flushing, increased sweating;
- high or low blood pressure;
- dizziness, vertigo or faintness;
- sore tongue or mouth, dry mouth, thirst, loss of appetite, weight loss, nausea (feeling sick), vomiting, stomach or abdominal pain, indigestion, gas, diarrhea, loose stools, constipation;
- muscle ache, pain or stiffness, joint pain, arthritis;
- irritability, anxiety, agitation, nervousness, mood swings, difficulty concentrating, lack of interest in life;
- loss of hair or change in hair;
- skin disorders, including itching or rash, dry skin, redness, brown spots on skin, increased or decreased sensitivity to touch, sensitivity to light, eczema, psoriasis;

- disorders of the respiratory tract, including hoarseness, sore throat, cough, runny nose, stuffy nose, sinus infection, bronchitis, pneumonia;
- viral or fungal infection, herpes simplex (fever blister); or
- menstrual disorder.

The most common side effects of VICTRELIS TRIPLE™ include:

- fatigue, low red blood cell count (anemia), change in sense of taste, nausea, headache, diarrhea, vomiting, abdominal pain, fever, muscle and joint pain, weight loss, difficulty in sleeping, and dry skin;
- fatigue, dizziness, fainting, changes in blood pressure, and blurred vision can occur, so be cautious before driving or operating heavy machinery.

Some patients may have: change in sense of taste or smell, inflammation, infection, pain, or dryness of the eye, tear disorder, blurred vision, earache, middle ear infection, allergic reaction, puffiness of hands and feet, inflamed or bleeding gums, tooth abscess, rectal sores, decreased sex drive, impotence, irritation of the vagina, migraine headache, gout, change in thyroid function.

Very rarely, cases of stroke (cerebrovascular events) have been reported.

Very rarely, peginterferon alfa-2b, alone or with ribavirin, may cause aplastic anemia. Aplastic anemia is a condition caused by the failure of the bone marrow to make new red blood cells, white blood cells and platelets. Pure red cell aplasia has also been reported. Pure red cell aplasia is a condition in which severe and sudden anemia (characterized by symptoms such as severe tiredness/fatigue, and shortness of breath on mild exertion) develops due to failure of the bone marrow to produce red blood cells.

Additionally, the following events have been reported with peginterferon alfa-2b: facial palsy (weakness and slumping on one side to the face), severe allergic reactions such as angioedema (an allergic skin disease characterized by patches of circumscribed swelling involving the skin and its subcutaneous layers, the mucous membranes, and sometimes the internal organs), toxic epidermal necrolysis/Stevens Johnson Syndrome/erythema multiforme (a spectrum of rashes with varying degree of severity including death which may be associated with blisters in the mouth, nose, eyes and other mucosal membranes and sloughing of the affected area of the skin) and blindness.

Additionally, Vogt-Koyanagi-Harada syndrome (an autoimmune inflammatory disorder affecting the eyes, skin and the membranes of the ears, brain

and spinal cord) has been reported with peginterferon alfa-2b use.

Tell your provider right away if you have any side effect that bothers you or that does not go away.

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 call your doctor or pharmacist
		Only if severe	In all cases	
Very common	Blood problems: low red cell counts (anemia) which may lead to tiredness, headaches, shortness of breath when exercising, dizziness and looking pale.		√	
	Blood problems: low white blood cell counts (neutropenia) which may lead to an increased risk of getting infections.		√	
Common	Mental health: depression, thoughts of suicide, experience hallucinations, aggressiveness or confusion, or have trouble sleeping or concentrating		√	
	Heart: chest pain, high or low blood pressure, changes in the way your heart beats		√	
	Infection: High fever or chills, or pain while urinating		√	
	Thyroid: new or worsening problems with thyroid function		√	
Uncommon	Blood sugar: high blood sugar or diabetes		√	
	Colitis (inflammation of the bowel): abdominal pain, bloody diarrhea, fever		√	
	Eye: change in vision such as decrease or loss of vision		√	
	Ear: hearing problem		√	
	Lung: trouble breathing, infection, pneumonia, inflammation of lung tissue, new or worse high blood pressure in the lung (pulmonary hypertension)		√	
	New or worsening rheumatoid arthritis, systemic lupus erythematosus, psoriasis		√	
	Women who are planning or become pregnant			√

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

HOW TO STORE IT

Storage of VICTRELIS TRIPLE™ Packages:

Store the VICTRELIS TRIPLE™ package refrigerated between 2°C and 8°C.

Storage of boceprevir:

Boceprevir Capsules should be refrigerated at 2°C–8°C until dispensed by a pharmacist. When separated and for patient use, refrigerated capsules of VICTRELIS™ can remain stable until the expiration date printed on the label.

VICTRELIS™ can also be stored at room temperature (15°C–30°C) for 3 months. Store in the original container.

Storage of ribavirin:

When separated, ribavirin capsules should be stored in the refrigerator between 2°C and 8°C or at controlled room temperature between 15°C and 30°C.

Stability and storage for peginterferon alfa-2b REDIPEN®:

Store the peginterferon alfa-2b REDIPEN® at 2°C to 8°C. Once reconstituted peginterferon alfa-2b REDIPEN® should be used immediately but may be stored at 2°C–8°C for up to 24 hours. Do not freeze.

Keep VICTRELIS TRIPLE™ and all medicines out of the reach and sight of children.

Do not use past expiry date on the label.

REPORTING SUSPECTED SIDE EFFECTS

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, Ontario 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.

or at Merck Canada Inc. by one of the following 2 ways:

- Call toll-free at 1-800-567-2594
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-496-9092, or
 - Mail to: Merck Canada Inc.
Pharmacovigilance
P.O. Box 1005
Pointe-Claire–Dorval, QC
H9R 4P8

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

MORE INFORMATION

For this document plus the full product monograph, prepared for health professionals, please contact the sponsor, Merck Canada Inc. at:
1-800-567-2594.

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Last revised: November 4th, 2011

