PART III: CONSUMER INFORMATION

PrEpoprostenol for Injection
(epoprostenol sodium)

This leaflet is part III of the "Product Monograph" published when Epoprostenol for Injection was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Epoprostenol for Injection.

Read all of this leaflet carefully before you start taking this medicine. Keep this leaflet. You may need to read it again. Contact your doctor, nurse or pharmacist if you have any questions about this medicine.

ABOUT THIS MEDICATION

Epoprostenol for Injection is a very complicated medication to administer. The drug must be prepared under rigorous conditions. You will need to learn about the medicine, the delivery system (the central venous catheter) and the pump. You will need to have a 'significant other' who is willing to learn along with you and to be available in case of need. Your doctor or nurse will teach you and your 'significant other' how to prepare the medication and use the pump for administering the medication.

What the medication is used for:
Epoprostenol for Injection is used to treat a lung condition called pulmonary arterial hypertension (PAH). This is where the pressure is high in the main blood vessels in the lungs.

What it does:
Epoprostenol for Injection widens the blood vessels to lower the blood pressure in the lungs.

When it should not be used:
Do not use Epoprostenol for Injection if you:
- are allergic (hypersensitive) to epoprostenol, the medicinal ingredient in Epoprostenol for Injection, to any other ingredient in the formulation (see "What the nonmedicinal ingredients are" below), or to similar medicines.
- have heart failure.
- had fluid in the lungs (pulmonary edema) when you were started on Epoprostenol for Injection.

If you think any of these apply to you, don't take Epoprostenol for Injection until you have checked with your doctor.

What the medicinal ingredient is:
epoprostenol sodium.

What the nonmedicinal ingredients are:
The nonmedicinal ingredients in Epoprostenol for Injection and the diluent are glycine, mannitol, sodium chloride, sodium hydroxide, and water for injection.

What dosage forms it comes in:
Epoprostenol for Injection comes as a powder in a glass vial. Each vial contains epoprostenol sodium equivalent to either 0.5 mg or 1.5 mg epoprostenol.

Sterile diluent for Epoprostenol for Injection is supplied in 50 mL glass vials.

WARNINGS AND PRECAUTIONS

BEFORE you use Epoprostenol for Injection talk to your doctor, nurse or pharmacist if you:
- have any problems with bleeding.
- are pregnant, or think you could be, or if you are planning to become pregnant. Your doctor will consider the benefit to you and the risk to your baby of taking Epoprostenol for Injection while you're pregnant.
- are breast-feeding. It is not known whether the ingredients of Epoprostenol for Injection can pass into breast milk.
- are younger than 18 years of age.

BEFORE you use Epoprostenol for Injection, the powder must be dissolved (reconstituted) in the specific liquid (Sterile Diluent) provided.

Driving and using machines: Pulmonary arterial hypertension and your treatment may have an effect on your ability to drive or use machinery. Don't drive or use machines unless you're feeling well.

Stopping Epoprostenol for Injection treatment must be done gradually. If the treatment is stopped too quickly, you may get serious side effects, including dizziness, feeling weak and breathing difficulties.

If you have problems with the infusion pump or injection line that stops, or prevents treatment with Epoprostenol for Injection, go to your hospital emergency department immediately.

Infection of the blood (sepsis/septicemia) is a serious common side effect in people taking Epoprostenol for Injection. Symptoms of sepsis include chills, with or without shaking, and fever. If you get any of these symptoms, go to your hospital emergency department immediately.

Avoid situations that can lower blood pressure, including saunas, sunbathing or hot baths.

Your doctor will arrange regular blood tests to check how well your blood clots.

INTERACTIONS WITH THIS MEDICATION

As with most medicines, interactions with other drugs are possible. Tell your doctor, nurse or pharmacist about all the medicines you take, including drugs prescribed by other doctors, vitamins, minerals, natural supplements, or alternative medicines.

Some medicines may affect how Epoprostenol for Injection works, or make it more likely that you'll have side effects. Epoprostenol for Injection can also affect how some other medicines work. These include:

- medicines used to prevent blood clots.
- medicines used to dissolve blood clots.
- medicines used for heart failure.
- medicines used for high blood pressure.
- medicines used for angina (chest pain).
- other medicines used to treat pulmonary arterial hypertension.
- medicines to treat inflammation or pain (also called 'NSAIDs').
- digoxin (a medicine used to treat heart disease).
- diuretics (water pill)

PROPER USE OF THIS MEDICATION

Usual adult dose:
Your doctor will decide how much (i.e. dose) and the duration of Epoprostenol for Injection therapy that is right for you. The amount you are given is based on your body weight, and your type of illness. Your dose may be increased or decreased depending on how well you respond to treatment.

Epoprostenol for Injection should only be given by slow continuous infusion (drip) into a vein.

Overdose:
Seek urgent medical attention if you think you have used too much Epoprostenol for Injection. Symptoms of overdose may include headache, nausea, vomiting, diarrhea, fast heart rate, warmth or tingling, or feeling like you might pass out (feeling faint/dizziness), unconsciousness, or collapse.

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.

Administration:
Initial Treatment
Your first treatment will be given to you in a hospital. This is because your doctor needs to monitor you and find the best dose for you.

You will start with an infusion of Epoprostenol for Injection. The dose will be increased, until your symptoms are relieved, and any side effects are manageable. Once the best dose has been found, a permanent tube (also referred to as a line or central venous catheter) will be fitted into one of the large veins in your upper chest called a central vein. This is done because Epoprostenol for Injection needs to be given by continuous controlled infusion.

Your doctor will decide which type of catheter is best suited for you. The catheter is a thin soft flexible tube that is inserted under a local anaesthetic in the operating room. Sterile conditions are maintained during this procedure to avoid the risk of infection. You will not feel it inside your body. The catheter has been tunnelled into place inside your chest. The catheter has a Dacron fibre cuff which is under the skin. This will hold the catheter in place and avoid infection. The catheter may also be sutured into position. The tip of the catheter lies in a vein that leads to the entrance of your heart. You can then be treated using an infusion pump that will deliver a prescribed amount of the drug through the catheter directly to your heart.

Your nurse will teach you how to care for the catheter, how to keep the skin around the catheter exit site clean and free from infection. You will learn how to change the dressing and to protect your skin. Your doctor and nurse will make sure that you are comfortable in caring for the catheter exit site. It is very important that you follow all of their instructions carefully (see 'Caring for the Central Venous Catheter' below).

Should you develop sudden fever, contact your doctor as soon as possible.

Continual Treatment
Your doctor or nurse will show you how to prepare and use Epoprostenol for Injection and will also advise you how to stop treatment if necessary. Stopping Epoprostenol for Injection must be done gradually. It is very important that you follow all their instructions carefully.

Steps for Reconstituting Epoprostenol for Injection
Epoprostenol for Injection comes as a powder in a glass vial. Before use, the powder must be dissolved (reconstituted) in the liquid (Sterile Diluent) provided and used as directed by your doctor. Epoprostenol for Injection should only be used with the supplies provided. Do not use Epoprostenol for Injection if solution shows haziness, particulate matter, discolouration, or leakage. The liquid does not contain a preservative. If you have any of the dose left over, it must be thrown away.

The following instructions explain how to reconstitute Epoprostenol for Injection. **They should supplement the instructions given to you by your doctor or nurse.**

Epoprostenol for Injection must be reconstituted with specific Sterile Diluent for Epoprostenol for Injection. Reconstituted Epoprostenol for Injection solution should not be mixed with other solutions or medicines prior to or during administration.

Your doctor will tell you how much Epoprostenol for Injection and Sterile Diluent you will need to use when making up your daily supply. The general procedures for reconstituting Epoprostenol for Injection solution are described below.

1. First, clean your worksite and gather your supplies. Wash your hands thoroughly and then open all the packages. Remove the vial caps from the vial containing specific Sterile Diluent for Epoprostenol for Injection and clean the tops of the vials with alcohol swabs.

2. Once you finish cleaning the tops of your vials and opening your supplies, attach a needle to the syringe. Now break the syringe seal by gently pulling the plunger out slightly and then pushing it back. Draw air into the

syringe; the amount of air that you draw into the syringe should be equal to the amount of Sterile Diluent you've been instructed to withdraw from the vial. Insert the needle through the rubber seal of the vial and press the plunger down to inject the air into the vial. Once all the air has been injected, pull the plunger gently back up to withdraw the prescribed amount of Sterile Diluent. Without withdrawing the needle, invert the vial and syringe and tap the syringe gently so that any air bubbles trapped in the syringe rise towards the top. If necessary, depress the plunger gently to force the air bubbles out and then withdraw sufficient additional Sterile Diluent to restore the required volume in the syringe. Once the required volume has been drawn into the syringe, withdraw the needle.

3. Now insert the needle through the rubber seal of the Epoprostenol for Injection vial and inject the Sterile Diluent gently onto the side of the vial. Always direct the flow of Sterile Diluent towards the side of the vial and inject it gently so that the Epoprostenol for Injection doesn't foam. Allow the pressure to equalize and withdraw the needle from the vial. Now, mix the Epoprostenol for Injection by gently swirling the vial. Turn the vial upside down to catch any undissolved powder near the top. **Never shake the vials.** If you need to mix more than one vial of Epoprostenol for Injection, simply repeat this process.

4. Your doctor or nurse will advise you on the amount of reconstituted Epoprostenol for Injection to be withdrawn. First, by gently pulling the plunger back, fill the syringe with the amount of air that is equal to the amount of Epoprostenol for Injection to be withdrawn. Remember to wipe the tops of the vials with an alcohol swab. Now, insert the needle through the seal of the Epoprostenol for Injection vial and inject the air. Then pull the plunger gently back to withdraw the reconstituted Epoprostenol for Injection into the syringe. Remove any air that may be trapped in the syringe as described in step 2 above. Withdraw the needle and place the cap back on the syringe.

5. You are now ready to inject the Epoprostenol for Injection into your cassette. Remove the end cap from the cassette tubing; then carefully remove the needle from the syringe, discard in an appropriate manner and attach the syringe to the cassette tubing. Now, while holding the cassette in one hand, you can use the tabletop as a third hand while you push down on the syringe to inject the solution into the cassette. Once the syringe is empty, clamp the cassette tubing near the syringe, disconnect the syringe and cap the tubing with the red cap.

6. Now you will withdraw the contents of the Sterile Diluent vials and inject them into the cassette. Using a 60 cc syringe, attach a new needle to the syringe, break the seal on the syringe by pulling the plunger out and pushing it back in. Next, fill the syringe with the amount of air that is equal to the amount of Sterile Diluent you will remove from the first vial. Remember to wipe the top of the Sterile Diluent vial with an alcohol swab before you insert the needle. Once it is dry, insert the needle through the rubber seal, inject some of the air into the vial and allow the fluid to flow into the syringe. With the larger syringe, it may be easier to hold it in the vertical position. Push more air in as needed until you have withdrawn all of the contents of the vial. Remove any air that may be in the syringe as described in step 2 above. Once the vial is emptied, allow the pressure to equalize before you pull the needle out. If you don't, you may lose fluid from the syringe or the vial and you would need to start the whole process over again. Withdraw the needle and place the cap back on the syringe.

7. Now you are ready to inject the first syringe full of Sterile Diluent into the cassette. To do this, first uncap the cassette tubing. Then carefully remove the needle from the syringe, discard in an appropriate manner and attach the syringe to the cassette tubing. Unclamp the cassette tubing and then carefully inject the solution into the cassette. When the syringe is empty, clamp the cassette tubing near the syringe, disconnect the syringe and cap the cassette tubing. You will repeat this same process to transfer the contents of the required Sterile Diluent vial as specified by your doctor or nurse into the cassette.

8. After you have completed the transfer of all the required Sterile Diluent, leave the syringe attached to the cassette tubing while you mix the solution. Gently invert the cassette at least 10 times, thoroughly mixing the Epoprostenol for Injection. Now you need to remove all the air from the cassette.

9. In order to remove the air inside the cassette, first you have to collect the air bubbles. Simply rotate the cassette around until all of the small bubbles join to form one big air pocket. Then tilt the cassette carefully so that the air pocket is in the corner where the tubing connects to the bag. To remove the air from the cassette, unclamp the tubing and pull back the plunger of the syringe until you see fluid fill the tubing. Then clamp the tubing near the connector, disconnect it and cap it with the red cap. To avoid any confusion, label the cassette with the date and time you made up the Epoprostenol for Injection.

Now put the cassette into the refrigerator until it is time to use it. Store it on the top shelf to avoid spilling any food or drink onto your cassette. Always have a back-up cassette that is ready for use.

Steps for Administering Epoprostenol for Injection for Injection by a Continuous Infusion Pump

You will use a pump to receive medication by continuous delivery. The instructions for use may vary depending on the particular make and model of the pump you are using. To avoid any potential interruptions in Epoprostenol for Injection delivery, you should have access to a back-up infusion pump and intravenous infusion sets.

Your doctor or nurse will give detailed instructions on how to use and care for the specific pump and accessories that you will use for administering the medicine (including changing the pump battery, cassette and tubing).

The temperature of the Epoprostenol for Injection solution inside the pump can be maintained for up to 48 hours at 2° to 8 °C with the use of a 'cold pouch' containing two frozen 6-oz gel packs. **Remember to change the gel packs every 12 hours or every 8 hours if room temperature approaches 25 °C. When stored or in use, Epoprostenol for Injection must not be exposed to light.**

Steps for Caring for the Central Venous Catheter
Change the dressing on the catheter exit site 1 to 2 times per week or more frequently if needed.

You will need the following equipment: dressing set, 2 sterile containers, povidone-iodine antiseptic solution, gauze swabs, 70% alcohol, povidone-iodine antiseptic ointment, sterile cotton swabs, adhesive tape (non-allergenic), transparent dressing 10 cm x 12 cm or 6 cm x 7 cm.

Maintain sterile technique at all times. If you suspect that you have contaminated anything, discard the equipment and begin again.

1. Assemble equipment.
2. Stabilize catheter while removing old transparent dressing.
3. Open sterile dressing kit.
4. Pour alcohol into sterile container.
5. Pour povidone-iodine antiseptic solution into sterile container.
6. Squeeze povidone-iodine antiseptic ointment onto sterile field.
7. Open transparent dressings onto sterile field.
8. Remove old transparent dressing.
9. Clean the catheter exit site with povidone-iodine antiseptic solution soaked 2" x 2" gauze swabs, starting at the catheter exit site. Work outward in a circular extending motion extending to an 8 cm radius.
10. Repeat step 9 three times.
11. **Never return to the catheter exit site using the same swab.**
12. Repeat steps 9 and 10 using an alcohol soaked 2" x 2" gauze swab.
13. Apply povidone-iodine antiseptic ointment to the catheter exit site with a sterile cotton swab.
14. Apply new sterile transparent dressing.
15. Tape catheter to skin using 'stress loop'.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:
- headache
- jaw pain
- diarrhea, nausea, vomiting
- stomach discomfort or pain, dry mouth
- pain (chest, bone, muscle and/or joint)
- feeling anxious, nervous, and/or agitated
- rash
- pain and/or redness at the injection site
- sweating, redness of your face (flushing)
- feeling tired, weak
- pale skin

If any of these affects you severely, tell your doctor, nurse or pharmacist.

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

Symptom / effect		Talk with your doctor, nurse or pharmacist		Seek immediate medical help
		Only if severe	In all cases	
Common	**Bleeding and decreased platelets:** bleeding that lasts longer than usual or which cannot be stopped, bruising more easily than normal. fatigue and weakness.		✓	
Common	**Low blood pressure or unusually fast or slow heart beat:** dizziness, fainting, lightheadedness may occur when you go from lying or sitting to standing up.	✓		
Common	**Blood infection (sepsis/septicemia):** chills, with or without shaking, and fever.			✓
Uncommon	**Build up of fluid in the lungs (pulmonary edema):** swelling or difficulty breathing.			✓
Rare	**Injection site infection:** redness, tenderness, swelling or pus at infusion site.			✓
Very Rare	**Ascites:** swelling due to build up of fluid around the stomach		✓	
Very Rare	**Hyperthyroid (overactive thyroid):** weight loss, fast heartbeat, sweating, frequent bowel movements, thin brittle hair and/or skin, sweating, anxiety, nervousness.		✓	
Very Rare	**Enlarged spleen:** upper left abdominal discomfort, fullness or pain, problems digesting a large meal.		✓	
Very Rare	**Injection site reaction:** tenderness, burning, stinging, swelling, redness, blistering or peeling.			✓
Very Rare	**Injection line blockage:** dizziness, weakness and breathing difficulties.			✓

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

Symptom / effect	Talk with your doctor, nurse or pharmacist		Seek immediate medical help
	Only if severe	In all cases	
Heart attack: Feeling of tightness around the chest; pain radiating into the arm or jaw combined with shortness of breath, nausea and lightheadedness.			✓
Too much pumping of blood from the heart (high cardiac output failure): Leading to persistent cough, shortness of breath, fatigue, swelling of the legs and abdomen due to fluid build-up		✓	

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

HOW TO STORE IT

Keep out of the reach and sight of children.

Do not use Epoprostenol for Injection after the expiry date on the label.

Store the vials of Epoprostenol for Injection at 15° to 25 °C. Protect from light by keeping Epoprostenol for Injection in its carton until it is used.

Store the vials of STERILE DILUENT for Epoprostenol for Injection at 15° to 25° C. **Do not freeze**.

Reconstituted Solution

Prior to use, reconstituted solutions of Epoprostenol for Injection must be protected from light and must be refrigerated at 2° to 8° C if not used immediately. Under these conditions, reconstituted Epoprostenol for Injection may be stored for up to 40 hours before being transferred to the infusion pump. Reconstituted Epoprostenol for Injection solution that has been transferred to the infusion pump within 40 hours (i.e. that has not been stored for more that 40 hours) may be used for no longer than 8 hours. **Do not freeze** reconstituted solutions of Epoprostenol for Injection. **When stored or in use, reconstituted Epoprostenol for Injection must not be exposed to direct sunlight. When administered at room temperature (up to 25°C), the reconstituted solutions may be used for no longer than 12 hours.**

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 https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html**
- **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 https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html.

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

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Sandoz Canada Inc., at:

1-800-361-3062

or by written request at:
110 rue de Lauzon
Boucherville QC
J4B 1E6

Or by e-mail at:
medinfo@sandoz.com

This leaflet was prepared by Sandoz Canada Inc.

Last revised: December 6, 2018