

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr**CARIPUL**[®]

Epoprostenol for Injection

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

CARIPUL[®] is a very complicated medication to administer. The drug must be prepared daily 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 healthcare professional will teach you and your ‘significant other’ how to prepare the medication and use the pump for administering the medication.

What is **CARIPUL[®] used for?**

CARIPUL[®] is used in adults (18 years of age and older) to treat a lung condition called pulmonary hypertension. This happens when there is high blood pressure in the main blood vessels in the lungs.

How does **CARIPUL[®] work?**

CARIPUL[®] widens the blood vessels to lower the blood pressure in the lungs.

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

Medicinal ingredient: epoprostenol sodium.

Non-medicinal ingredients: L-arginine, sodium hydroxide, and sucrose.

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

Powder for Solution: 0.5 mg/vial and 1.5 mg/vial of epoprostenol (as epoprostenol sodium).

Do not use **CARIPUL[®] if:**

- you have or previously developed pulmonary edema (fluid in your lungs) after starting **CARIPUL**[®] treatment (See the **Serious side effects and what to do about them** table below for more information).
- you are allergic to epoprostenol sodium, any of the other ingredients in **CARIPUL**[®], or to similar medicines.
- you have heart failure.

If you think any of these apply to you, don't take **CARIPUL**[®] until you have checked with your healthcare professional.

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

- have any problems with bleeding.
- are pregnant, or think you could be, or if you are planning to become pregnant. Your healthcare professional will consider the benefit to you and the risk to your baby of taking CARIPUL® while you're pregnant.
- are breast-feeding. It is not known whether the ingredients of CARIPUL® can pass into breast milk.

Other warnings you should know about:

- Pulmonary 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 CARIPUL® 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 CARIPUL®, go to your hospital emergency department immediately.
- Infection of the blood (sepsis/septicemia) is a serious common side effect in people taking CARIPUL®. 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.
- CARIPUL® can cause low blood pressure that can be severe. You should avoid situations that can lower your blood pressure, including saunas, sunbathing, or hot baths. Symptoms of low blood pressure include feeling faint or lightheaded. If you get any of these symptoms, talk to a healthcare professional right away.
- A buildup of fluid in the abdomen (ascites) is a serious side effect in people taking CARIPUL®. Symptoms include swelling around the stomach, abdominal pain, a feeling of fullness and/or a flat or pushed out navel. If you get any of these symptoms, talk to a healthcare professional right away.
- Your healthcare professional will arrange regular blood tests to check how well your blood clots.

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

The following may interact with CARIPUL®:

- 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 hypertension.

- medicines to treat inflammation or pain (also called non-steroidal anti-inflammatory drugs or 'NSAIDs').
- digoxin, a medicine used to treat heart disease.
- diuretics (water pill), used to lower fluid levels (e.g., furosemide).

How to take CARIPUL®:

- **Initial Treatment**

Your first treatment will be given to you in a hospital. This is because your healthcare professional needs to monitor you and find the best dose for you.

You will start with an infusion of CARIPUL®. 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 CARIPUL® needs to be given by continuous controlled infusion.

Your healthcare professional 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 healthcare professional 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 healthcare professional 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 "**Steps for Caring for the Central Venous Catheter**" below).

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

- **Continual Treatment**

Your healthcare professional will show you how to prepare and use CARIPUL® and will also advise you how to stop treatment if necessary. Stopping CARIPUL® must be done gradually. It is very important that you follow all their instructions carefully.

Steps for Reconstituting CARIPUL®

CARIPUL® comes as a powder in a glass vial. Before use, the powder must be:

- dissolved (reconstituted) in vial with only 5 mL of either Sterile Water for Injection or Sodium Chloride 0.9% Injection.
- reconstituted product should be further diluted as directed with the same diluent used for reconstitution.
- CARIPUL® solution reconstituted with 5 mL Sterile Water for Injection or Sodium Chloride 0.9% Injection, and immediately diluted to the final concentration in the drug delivery reservoir can be administered per the conditions of use as outlined below:

Final concentration range	Immediate administration	If stored for up to 8 days at 2° - 8°C
≥3,000 ng/mL and <15,000 ng/mL	48 hours	24 hours
≥15,000 ng/mL	48 hours	48 hours

The following instructions explain how to reconstitute CARIPUL®. **They should supplement the instructions given to you by your healthcare professional.**

CARIPUL® must be reconstituted with Sterile water for injection or 0.9% Sodium Chloride injection solution. Reconstituted CARIPUL® solution should not be mixed with other solutions or medicines prior to or during administration.

Your healthcare professional will tell you how much CARIPUL® and Sterile Diluent you will need to use when making up your daily supply. The general procedures for reconstituting CARIPUL® 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 Sterile Diluent 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 CARIPUL® 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 CARIPUL® doesn't foam. Allow the pressure to equalize and withdraw the needle from the vial. Now, mix the CARIPUL® 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 CARIPUL®, simply repeat this process.
4. Your healthcare professional will advise you on the amount of reconstituted CARIPUL® 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 CARIPUL® to be withdrawn. Remember to wipe the tops of the vials with an alcohol swab. Now, insert the needle through the seal of the CARIPUL® vial and inject the air. Then pull the plunger gently back to withdraw the reconstituted CARIPUL® 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 CARIPUL® 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 healthcare professional 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 CARIPUL®. 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 CARIPUL®.

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.

Steps for Administering CARIPUL® 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 CARIPUL® delivery, you should have access to a back-up infusion pump and intravenous infusion sets.

Infusion sets with an in-line 0.22 micron filter should be used.

Suitable ambulatory pumps to be used for the administration of CARIPUL® include:

- CADD-Solis VIP

Manufactured by Smiths Medical.

Pump accessories found compatible with the administration of CARIPUL® include:

- CADD disposable Medication Cassette Reservoir 100 mL from Smiths Medical.
- CADD extension set with in-line 0.2 micron filter (CADD extension set with male luer, 0.2-micron air-eliminating filter, clamp, and integral anti-siphon valve with male luer) from Smiths Medical.

Your healthcare professional 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).

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 (nonallergenic), 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'.

Usual dose:

Your healthcare professional will decide how much (i.e. dose) and the duration of CARIPUL® 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.

CARIPUL® is given by slow continuous infusion (drip) into a vein.

Overdose:

Symptoms of an 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.

If you think you, or a person you are caring for, have taken too much CARIPUL®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using CARIPUL®?

These are not all the possible side effects you may feel when taking CARIPUL®. If you experience any side effects not listed here, tell your healthcare professional.

Side effects of CARIPUL® can include:

- headache
- jaw pain
- pain
- being sick (vomiting)
- feeling sick (nausea)
- diarrhea
- redness of your face (flushing)
- stomach discomfort or pain
- joint pain
- feeling anxious, feeling nervous
- rash
- pain at the injection site
- sweating
- dry mouth
- feeling tired, weak
- feeling agitated
- pale skin
- redness at the injection site
- overactive thyroid gland

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Chest pain			✓

Hypotension (low blood pressure): Unusually slow or fast heartbeats, or feeling dizzy or faint.			✓
Sepsis or septicemia (blood infection): chills, with or without shaking, fever, dizziness, high or very low body temperature, low blood pressure, heart palpitations, rapid breathing, or rapid heartbeat.			✓
Thrombocytopenia (low blood platelets): bleeding that lasts longer than usual or which cannot be stopped, bruising more easily than normal, fatigue, or weakness.		✓	
UNCOMMON			
Pulmonary edema (build up of fluid in the lungs): swelling, difficulty breathing, extreme shortness of breath, wheezing, gasping for breath, cold clammy skin, irregular heartbeat, cough that produces frothy sputum, or blue-tinged lips.			✓
RARE			
Injection site infection: redness, tenderness, swelling, or pus at infusion site.		✓	
VERY RARE			
Ascites (fluid in the abdomen): swelling around the stomach, abdominal pain, feeling of fullness, flat or pushed out navel, increase in weight, or shortness of breath.		✓	
High cardiac output failure (heart is unable to pump sufficient blood for the body): persistent cough, shortness of breath, fatigue, or swelling of the legs and abdomen due to fluid build-up.			✓
Injection line blockage: dizziness, weakness, or breathing difficulties.			✓
Injection site reaction: tenderness, burning, stinging, swelling, redness, blistering, or peeling.		✓	
Myocardial infarction (heart attack): feeling of tightness around the chest, pain radiating into the arm or jaw combined with shortness of breath, nausea, light-headedness, or dizziness.			✓
Splenomegaly (enlarged spleen): upper left abdominal discomfort or		✓	

pain, feeling of fullness, problems digesting a large meal, fatigue, or frequent infections.			
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If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

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

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) 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 professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store the unopened vials of CARIPUL® between 15°C and 30°C. Protect from freezing.
- Do not use CARIPUL® after the expiry date on the label.
- Follow hospital rules when throwing away unused drug and other waste.

Do not expose reconstituted or diluted CARIPUL® solution to direct sunlight.

Keep out of reach and sight of children.

If you want more information about CARIPUL®:

- Talk to your healthcare professional.
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (www.janssen.com/canada) or by calling 1-800-567-3331 or 1-800-387-8781.

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