A step-by-step preparation guide

What is VELETRI® (epoprostenol) for Injection?
VELETRI is a prescription medicine that is given intravenously (in a vein). It is used to treat adults with certain kinds of severe pulmonary arterial hypertension (PAH) (WHO Group 1), a condition in which blood pressure is too high in the blood vessels between the heart and the lungs. VELETRI may improve your ability to exercise as measured by how far you can walk in 6 minutes (6-minute walk test).

Studies showing VELETRI is effective included mainly patients with NYHA Functional Class III-IV PAH. In these patients, PAH was caused by unidentified or hereditary factors or connective tissue disease.

Who should not take VELETRI?
VELETRI should not be used if you have heart failure due to severe left heart disease, if you develop fluid in the lungs (pulmonary edema) when starting therapy, or if you are allergic to epoprostenol.

Some medications may interact with VELETRI. Please talk to your doctor about all of your medications.

Please see Important Safety Information on page 2 and on page 25. Please see accompanying full Prescribing Information on front of easel.

Learn more at www.veletri.com
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Who should not take VELETRI?
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Some medications may interact with VELETRI. Please talk to your doctor about all of your medications.

What is the most important information I should know about VELETRI?
It is important to use VELETRI as directed by your doctor. VELETRI should be used only with Sterile Water for Injection, USP, or Sodium Chloride 0.9% Injection, USP. Do not mix VELETRI with other intravenous medications. Each vial is for single use only; discard any unused medication. Use at room temperature (77°F/25°C). Do not expose VELETRI to direct sunlight.

When you take epoprostenol for the first time, you must be in a setting (hospital or clinic) where you can be monitored for any serious side effects or in case of emergency. Your blood pressure and heart rate should also be monitored with any dose changes. If you are taking VELETRI, your doctor may prescibe another kind of medicine used to prevent blood clots. It is the use of these medications concomitantly (in combination) with VELETRI that may potentially cause an increase in the risk of bleeding.

Sudden and dramatic changes in dose may lead to unstable blood pressure, a return of pulmonary hypertension symptoms, or fatal low blood pressure (hypotension). Do not stop using VELETRI without first talking to your doctor.

To reduce the risk of infection in the bloodstream, it is important to know how to properly care for the catheter and infusion pump.

What are the possible side effects of VELETRI?
You may have side effects at the start of treatment or with dose increases. The most common side effects seen in at least 1% of patients were flushing, headache, nausea/vomiting, low blood pressure, anxiety/nervousness, chest pain, dizziness, slow heartbeat, abdominal pain, pain in the muscles and/or ligaments and bones, shortness of breath, back pain, sweating, upset stomach, numbness/increased sensitivity, and fast heartbeat.

The most common side effects in patients with PAH due to unidentified or hereditary factors with at least 10% difference between the group that received epoprostenol and the group that received conventional therapy alone were flu-like symptoms, fast heartbeat, flushing, diarrhea, nausea/vomiting, jaw pain, pain in the muscles and/or ligaments and bones, anxiety/nervousness, dizziness, headache, and numbness/increased sensitivity/tingling.

The most common side effects in patients with PAH due to connective tissue disease with at least 10% difference between the group that received epoprostenol and the group that received conventional therapy alone were flushing, low blood pressure, lack of appetite, nausea/vomiting, diarrhea, jaw pain, neck/joint pain, headache, skin ulcer, and rash.

Talk to your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of VELETRI. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see accompanying full Prescribing Information on front of easel.
Storage of prepared medication

The instructions in this guide must be followed to ensure that the drug retains its stability and that the proper dose is delivered.

- Mixed (reconstituted) or diluted medication should be protected from direct sunlight
- Dilute immediately after reconstitution. Do not store reconstituted medication in the vial
- Fully diluted cassettes may be stored for up to 8 days in the refrigerator (36°F to 46°F/2°C to 8°C). Your healthcare professional or specialty pharmacy nurse will direct you on how to store your prepared medication

Your healthcare professional will determine the best concentration, storage, and administration schedule for you.

For more information about storing VELETRI® (epoprostenol) for Injection, please refer to the accompanying full Prescribing Information on front of easel and talk to your healthcare professional.
Your VELETRI continuous administration system

The VELETRI® (epoprostenol) for Injection administration system is designed to maintain continuous, steady VELETRI dosing, 24 hours a day, at the concentration prescribed by your physician.
Preparing the work area

This is a very important step because bacterial contamination can lead to serious infections in individuals on intravenous drug therapy.

To help prevent infection, clean the area where you will be preparing VELETRI® (epoprostenol) for Injection with disinfectant wipes or 70% alcohol. Let the surface air-dry. Follow these directions again if the area becomes contaminated during use.

Also, thoroughly wash your hands with soap and warm water for at least one minute, and then dry prior to reconstituting, diluting, and administering VELETRI. If you must leave the work area before completing the process, be sure to **thoroughly wash and dry your hands again.**
Needle system

**Identifying and gathering equipment**

Make sure you have all the necessary supplies gathered in your work area prior to beginning. Generally, these supplies include:

A. Vial(s) of VELETRI® (epoprostenol) for Injection 0.5 mg or 1.5 mg powder

   Two 50-mL vials of either

B1. Sterile Water for Injection, USP

B2. Sodium Chloride 0.9% Injection, USP (normal saline)

C. One 100-mL medication cassette

D. 60-mL syringe

E. 18-gauge needle(s)

F. 5-mL or 10-mL syringe with needle

G. Three alcohol pads

H. Sharps container

I. Extension tubing with 0.22 micron filter

J. Pump

K. Cassette labels

*Please ask your specialty pharmacy about the availability of a needle-free system.*
Step-by-step instructions:

Mixing (reconstitution) using the needle system

1. Wash your hands and clean your work surface with disinfectant wipes or 70% alcohol. See page 5 for detailed instructions.

2. Remove the caps from the vial of VELETRI® (epoprostenol) for Injection and from the normal saline (NS) or sterile water (SW).
   If you are using the 0.5 mg vial of VELETRI, the cap will be white.

3. Clean the rubber stoppers of the vials of VELETRI and NS or SW with a disinfectant or antiseptic pad, or a pad with 70% alcohol.

Important: VELETRI is stable only when reconstituted as directed using Sterile Water for Injection, USP, or Sodium Chloride 0.9% Injection, USP. VELETRI must not be reconstituted or mixed with any other intravenous medications or solutions prior to or during administration. The same solution must be used for both reconstituting and diluting VELETRI. Do not combine sterile water with normal saline when preparing VELETRI.

These solutions are commercially available and can be purchased from either regular or specialty pharmacies.
Step-by-step instructions:
Mixing (reconstitution) using the needle system (continued)

4. Hold the 5-mL or 10-mL syringe with needle and draw back the plunger to the 5-mL mark to draw in air. 
   Be careful to avoid touching the plunger shaft. 
   Confirm that the needle is tightly attached to the syringe before removing the needle cap.

5. Insert the needle's tip bevel up (see inset) into the NS or SW vial at a 45-degree angle. Push the needle into the core of the vial. Press down on the plunger to inject the air from the syringe into the solution.

6. With the needle still inserted into the vial, turn the vial upside down. 
   Position the needle tip below the fluid level, and draw the prescribed amount of NS or SW into the syringe.
Step-by-step instructions:
Mixing (reconstitution) using the needle system (continued)

7. Gently pull the syringe out of the vial.

8. To add the prescribed amount of NS or SW to the powdered VELETRI® (epoprostenol) for Injection medication vial, insert the needle’s tip bevel up (see inset) at a 45-degree angle into the rubber stopper.

9. Slowly inject the NS or SW, making sure to prevent turbulence and foaming of the medication.
Step-by-step instructions:
Mixing (reconstitution) using the needle system (continued)

Do not shake. Gently roll the vial of VELETRI® (epoprostenoil) for Injection in your hands until the powder is completely dissolved and the solution is clear.

Turn the vial upside down to trap any undissolved powder that may be present near the top of the vial. Cloudiness and particles should not be present in the solution.

Draw back the appropriate amount of medication from the vial into the 5-mL or 10-mL syringe based on the desired concentration.

Recap the syringe and put it down on your clean work surface. You are now ready to fill the medication cassette.

Note: Please be cautious when re-capping the needle. As there are alternatives to re-capping the needle, please discuss this step with your healthcare professional.

Repeat steps 2 through 11 if more than one vial of VELETRI is being used.

Important: VELETRI is stable only when reconstituted as directed using Sterile Water for Injection, USP, or Sodium Chloride 0.9% Injection, USP. VELETRI must not be reconstituted or mixed with any other intravenous medications or solutions prior to or during administration. The same solution must be used for both reconstituting and diluting VELETRI. Do not combine sterile water with normal saline when preparing VELETRI.

These solutions are commercially available and can be purchased from either regular or specialty pharmacies.
Step-by-step instructions:

Diluting the medication and filling the medication cassette: needle system

1. Attach an 18-gauge needle to a 60-mL syringe and pull back the plunger to the 50-mL mark. Insert the needle into the stopper on the vial of NS or SW.

2. Inject air into the NS or SW bottle until you feel resistance.
   **Be careful to avoid touching the plunger shaft.**

3. Place the needle tip below the fluid surface; the air you injected into the bottle will draw fluid into the syringe. You may need to inject air into the bottle 2 or 3 times to draw the desired amount* of NS or SW. Once you have the desired amount of fluid drawn, remove the needle.

*Desired amount is 50 mL minus the mL amount of VELETRI® (epoprostenol) for Injection drawn earlier in Reconstitution step 11. For example, if 5 mL of VELETRI was used in step 11, then 45 mL of NS or SW should be drawn up for step 3 above.

Note: The same solution must be used for both reconstituting and diluting VELETRI® (epoprostenol) for Injection. Do not combine sterile water with normal saline when preparing VELETRI.
Next, remove the cap from the end of the medication cassette and place it on your clean work surface. Make sure you do not drop the cap, because it could become contaminated. Be careful not to touch the end of the exposed tubing.

Add the NS or SW to the cassette by screwing the syringe onto the end of the tubing.

**Note:** Close the slide clamp on the reservoir tubing after filling it with solution; otherwise, the medication will flow out.

Remove the empty syringe by unscrewing it.

Next, remove the needle from the syringe containing VELETRI® (epoprostenol) for Injection. Attach the syringe to the tubing on the medication cassette. Unclamp the tubing and inject the drug into the medication cassette. Recap the end and close the slide clamp of the cassette tubing.
Step-by-step instructions:
Diluting the medication and filling the medication cassette: needle system (continued)

7
Repeat dilution steps 1 through 5 with a second vial of NS or SW, drawing up a total of 50 mL of fluid. The total volume in the medication cassette will then equal 100 mL.

8
To remove excess air, tilt the cassette so that large air bubbles rise to the corner of the cassette where the tubing is attached.

9
Unclamp the tubing to remove air from the cassette. Pull back the plunger until ALL the air is removed from the cassette and tubing.
Clamp the tubing and remove the syringe from the cassette tubing; then attach the new sterile cap that was provided in the package.

Discard all used needles and any other sharp materials in a sharps container.
Each vial is for single use only. Discard any unused VELETRI® (epoprostenol) for Injection solution.

Connect the cassette by fitting the hooks onto the pivot pins at the base of the pump. Push the cassette up against the pump. Place the joined pump and cassette in an upright position on a steady surface. Secure the cassette by using a coin to turn the lock knob 90° counterclockwise until you feel it stop.

For more information about storing VELETRI, please refer to the accompanying full Prescribing Information on front of easel and talk to your healthcare professional.
Preparing the work area

This is a very important step because bacterial contamination can lead to serious infections in individuals on intravenous drug therapy.

To help prevent infection, clean the area where you will be preparing VELETRI® (epoprostenol) for Injection with disinfectant wipes or 70% alcohol. Let the surface air-dry. Follow these directions again if the area becomes contaminated during use.

Also, thoroughly wash your hands with soap and warm water for at least one minute, and then dry prior to reconstituting, diluting, and administering VELETRI. If you must leave the work area before completing the process, be sure to thoroughly wash and dry your hands again.

Decrease the chance of infection by keeping your work area clean.
Identifying and gathering equipment

Make sure you have all the necessary supplies gathered in your work area prior to beginning. Generally, these supplies include:

A Vial(s) of VELETRI® (epoprostenol) for Injection
   0.5 mg or 1.5 mg powder

B1 Two 50-mL vials of either
   Sterile Water for Injection, USP
B2 Sodium Chloride 0.9% Injection, USP (normal saline)

C One 100-mL medication cassette

D 60-mL syringe

E Mini-Spike vented dispensing pins

F 5-mL or 10-mL syringe

G Three alcohol pads

H Extension tubing with 0.22 micron filter

I Pump

J Cassette labels
Step-by-step instructions:
Mixing (reconstitution) using the needle-free system

1. Wash your hands and clean your work surface with disinfectant wipes or 70% alcohol. See page 15 for detailed instructions.

2. Remove the caps from the vial of VELETRI® (epoprostenol) for Injection and from the normal saline (NS) or sterile water (SW). If you are using the 0.5 mg vial of VELETRI, the cap will be white.

3. Clean the rubber stoppers of the vials of VELETRI and NS or SW with a disinfectant or antiseptic pad, or a pad with 70% alcohol.

Important: VELETRI is stable only when reconstituted as directed using Sterile Water for Injection, USP, or Sodium Chloride 0.9% Injection, USP. VELETRI must not be reconstituted or mixed with any other intravenous medications or solutions prior to or during administration. The same solution must be used for both reconstituting and diluting VELETRI. Do not combine sterile water with normal saline when preparing VELETRI.

These solutions are commercially available and can be purchased from either regular or specialty pharmacies.
Step-by-step instructions:
Mixing (reconstitution) using the needle-free system (continued)

4
Remove two Mini-Spike Dispensing Pins from the sterile packaging. Do not touch the spikes or the threaded connectors.

5
Insert one Mini-Spike into the rubber stopper on the vial of NS or SW and push it down until it clicks into place. Insert the other Mini-Spike into the rubber stopper on the vial of powdered VELETRI® (epoprostenol) for Injection medication and push it down until it clicks into place. Place the vials on your clean work surface.

6
Be careful to avoid touching the plunger shaft.
Screw the 5-mL or 10-mL syringe onto the threaded connector on the top of the Mini-Spike attached to the vial of NS or SW.

With the syringe attached to the vial, turn the vial upside down.
Pull the plunger back and draw the prescribed amount of NS or SW into the syringe.
Step-by-step instructions:
Mixing (reconstitution) using the needle-free system (continued)

Unscrew the syringe.

Screw the syringe filled with NS or SW to the threaded connector on top of the Mini-Spike attached to the vial of VELETRI® (epoprostenol) for Injection.

With the syringe attached to the vial, turn the vial upside down. Slowly inject the NS or SW, making sure to prevent turbulence and foaming of the medication.
Step-by-step instructions:
Mixing (reconstitution) using the needle-free system (continued)

10. **Do not shake.** Gently roll the vial of VELETRI® (epoprostenol) for Injection in your hands until the powder is completely dissolved and the solution is clear.

Keeping the syringe and the Mini-Spike together, turn the vial upside down to trap any undissolved powder that may be present near the top of the vial. Cloudiness and particles should not be present in the solution.

11. Draw back the appropriate amount of medication from the vial into the 5-mL or 10-mL syringe based on the desired concentration.

Unscrew the syringe and place it on your clean work surface. You are now ready to fill the medication cassette.

Repeat steps 2 through 11 if more than one vial of VELETRI is being used.

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Step-by-step instructions:

Diluting the medication and filling the medication cassette: needle-free system

Remove a Mini-Spike from the sterile packaging. **Do not touch the spike or the threaded connector.** Insert the spike into the rubber stopper on the vial of NS or SW and push it down until it clicks into place. Screw the 60-mL syringe onto the threaded connector on the top of the Mini-Spike.

With the syringe attached to the vial, turn the vial upside down. Pull the plunger back to withdraw the desired amount of fluid.* Then, unscrew the syringe from the Mini-Spike.

*Desired amount is 50 mL minus the mL amount of VELETRI drawn earlier in **Reconstitution step 11.** For example, if 5 mL of VELETRI was used in step 11, then 45 mL of NS or SW should be drawn up for step 2 above.

Next, remove the cap from the end of the medication cassette and place it on your clean work surface. Make sure you do not drop the cap, because it could become contaminated. Be careful not to touch the end of the exposed tubing.

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Note: The same solution must be used for both reconstituting and diluting VELETRI® (epoprostenol) for Injection. Do not combine sterile water with normal saline when preparing VELETRI.
Step-by-step instructions:

Diluting the medication and filling the medication cassette: needle-free system (continued)

Add the NS or SW to the cassette by screwing the syringe onto the end of the tubing.

Note: Close the slide clamp on the reservoir tubing after filling it with solution; otherwise, the medication will flow out.

Remove the empty syringe by unscrewing it.

Next, attach the syringe containing VELETRI® (epoprosteno) for Injection to the tubing on the medication cassette. Unclamp the tubing and inject the drug into the medication cassette. Recap the end and close the slide clamp of the cassette tubing.

Repeat dilution steps 1 through 4 with a second vial of NS or SW, drawing up a total of 50 mL of fluid. The total volume in the medication cassette will then equal 100 mL.
Step-by-step instructions:

Diluting the medication and filling the medication cassette: needle-free system (continued)

7. To remove excess air, tilt the cassette so that large air bubbles rise to the corner of the cassette where the tubing is attached.

8. Unclamp the tubing to remove air from the cassette. Pull back the plunger until ALL the air is removed from the cassette and tubing.

9. Clamp the tubing and remove the syringe from the cassette tubing; then attach the new sterile cap that was provided in the package.

Each vial is for single use only. Discard any unused VELETRI® (epoprostenol) for Injection solution.
Step-by-step instructions:

Diluting the medication and filling the medication cassette: needle-free system (continued)

Connect the cassette by fitting the hooks onto the pivot pins at the base of the pump. Push the cassette up against the pump. Place the joined pump and cassette in an upright position on a steady surface. Secure the cassette by using a coin to turn the lock knob 90° counterclockwise until you feel it stop.

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VELETRI should not be used if you have heart failure due to severe left heart disease, if you develop fluid in the lungs (pulmonary edema) when starting therapy, or if you are allergic to epoprostenol.

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When you take epoprostenol for the first time, you must be in a setting (hospital or clinic) where you can be monitored for any serious side effects or in case of emergency. Your blood pressure and heart rate should also be monitored with any dose changes. If you are taking VELETRI, your doctor may prescribe another kind of medicine used to prevent blood clots. It is the use of these medications concomitantly (in combination) with VELETRI that may potentially cause an increase in the risk of bleeding.

Sudden and dramatic changes in dose may lead to unstable blood pressure, a return of pulmonary hypertension symptoms, or fatal low blood pressure (hypotension). Do not stop using VELETRI without first talking to your doctor.

To reduce the risk of infection in the bloodstream, it is important to know how to properly care for the catheter and infusion pump.

What are the possible side effects of VELETRI?
You may have side effects at the start of treatment or with dose increases. The most common side effects seen in at least 1% of patients were flushing, headache, nausea/vomiting, low blood pressure, anxiety/nervousness, chest pain, dizziness, slow heartbeat, abdominal pain, pain in the muscles and/or ligaments and bones, shortness of breath, back pain, sweating, upset stomach, numbness/increased sensitivity, and fast heartbeat.

The most common side effects in patients with PAH due to unidentified or hereditary factors with at least 10% difference between the group that received epoprostenol and the group that received conventional therapy alone were flu-like symptoms, fast heartbeat, flushing, diarrhea, nausea/vomiting, jaw pain, pain in the muscles and/or ligaments and bones, anxiety/nervousness, dizziness, headache, and numbness/increased sensitivity/tingling.

The most common side effects in patients with PAH due to connective tissue disease with at least 10% difference between the group that received epoprostenol and the group that received conventional therapy alone were flushing, low blood pressure, lack of appetite, nausea/vomiting, diarrhea, jaw pain, neck/joint pain, headache, skin ulcer, and rash.

Talk to your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of VELETRI. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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