

“SQ” Prostacyclin Therapy

A guide for new medication starts

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Pulmonary Hypertension: What is it?

An overview

Pulmonary hypertension (PH) is another name for high blood pressure in the lungs. It is a big word, but let’s break it down. “Pulmonary” means lungs, and hypertension means “high blood pressure.” The high blood pressure in the lungs occurs because the arteries narrow down causing higher blood pressures. This higher pressure in the lungs makes the right side of the heart work harder to push blood through the lungs. This extra work causes the heart to become less flexible and even get bigger over time.

SYMPTOMS

Symptoms may include being unable to perform exercise or do activities that are normal for age. Increased tiredness, shortness of breath, dizziness, upset stomach, decreased appetite, and swelling of the face hands, and feet are commonly seen.

TESTING

Your doctor may order an echocardiogram (ultrasound of the heart), chest x-ray, or MRI (pictures of the heart by a magnetic field and radio waves). They could order a cardiac catheterization. This procedure directly measures the pressures and flow in the heart.



Pulmonary Hypertension

An overview of the disease, symptoms, & testing



Treatment options



Pain Management Strategies



Frequently Asked Questions: Things I Wish I knew

TREATMENT OPTIONS

Treatment for PH includes medications which can be given by mouth, inhaled, and/or continuously via a pump through an IV or under the skin (subcutaneously). For this guide, we will be focusing on SQ prostacyclin therapy.



Prostacyclin Therapy

What is a prostacyclin?

Prostacyclin is a normal compound found in everyone. It relaxes the smooth muscle of blood vessels, which then lowers the blood pressure including the blood pressure of the lungs. It is also normally responsible for keeping blood (platelets) from sticking to each other. In children with pulmonary hypertension, studies have suggested that there is a lower amount of prostacyclin in the blood (Vera Moulton Pulmonary Vascular Center, n.d.).

Prostacyclin was discovered by Sir John Vane in the 1970s, for which he won the Nobel Prize in Medicine. However, it was not until 1995 that the first prostacyclin analogue (epoprostenol) was approved by the FDA.

How do the medications work?

Prostacyclin medications for pulmonary hypertension work in two ways:

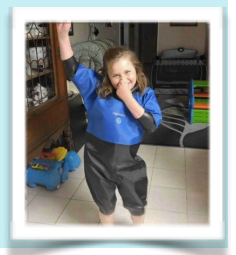
1. Directly stimulate the body to make more natural prostacyclin (selexipag)
2. Increase the total prostacyclin amount in the body by giving synthetic (or laboratory created) prostacyclin (epoprostenol, treprostinil, iloprost)

The end result is a higher prostacyclin concentration in the body, which relaxes blood vessels in the lungs and allows them to open up for blood flow.

WHAT I WISH I KNEW: MESSAGES FROM PARENTS

"Knowing what works for one person's child, may not work for yours. It is trial and error as you and your child get to know the process."

"Try to remain calm when putting in sites. The child will feel your stress so prepare [everything] first and then engage your child."



What types of prostacyclins are available today?

Drug Name (Generic/Brand Name)	FDA Approval	How it is Given	Frequency	Important Considerations
Epoprostenol (Flolan®)	1995	Intravenous	Continuous	New diluent allows it to be room temperature stable. Medication should never be flushed through IV line and never be abruptly stopped.
Epoprostenol (Veletri®)	2010	Intravenous	Continuous	Do not expose to direct sunlight. Never flush medication through an IV line and never abruptly stop the medication.
Treprostinil (Remodulin®) SQ "subcutaneous"	2002	Subcutaneous	Continuous	Syringe changes every 2-3 days depending on dose and concentration.
Treprostinil (Remodulin®) IV "intravenous"	2004	Intravenous	Continuous	Medication should never be flushed through central line. Half life of medication is 3-4 hours.
Treprostinil (Tyvaso®)	2009	Inhaled	Four times a day	It can only be used with Tyvaso inhalation system. Device components must be cleaned daily.
Iloprost (Ventavis®)	2004	Inhaled	Six to nine times a day	Can only be given through the I-neb AAD System
Treprostinil (Orenitram®)	2013	Oral	Two to three times a day	Take with food.
Selexipag (Uptravi®)	2015	Oral	Twice a day	May be taken with food if upset stomach occurs.

Subcutaneous Prostacyclin



What is it?

For children with more advanced disease or more serious symptoms, prostacyclin therapies may be considered. Inhaled and oral medications may have limitations of age, cooperation and dosing. In certain cases, continuous prostacyclin may be recommended by your child's medical team.

Subcutaneous ("SQ") treprostinil (also known by the brand name, Remodulin®) is the most commonly used continuous prostacyclin in children. This medication is given through a catheter under the skin that is hooked up to a pump filled with treprostinil. The pump runs continuously, so the child is always connected to it.

The "SQ" catheter placement and pump programming are managed by parents at home. There are three different catheter systems that you can choose from to increase your child's comfort level. The pump is small and discreet, making it a popular option for many families.

Intravenous ("IV") treprostinil or epoprostenol therapy are also treatments used in children. Reasons to choose this route over "SQ" include frequent skin irritations/infections, poor medication absorption or difficulties with treatment administration at home. Your medical team will discuss these concerns with you if they apply to your child.



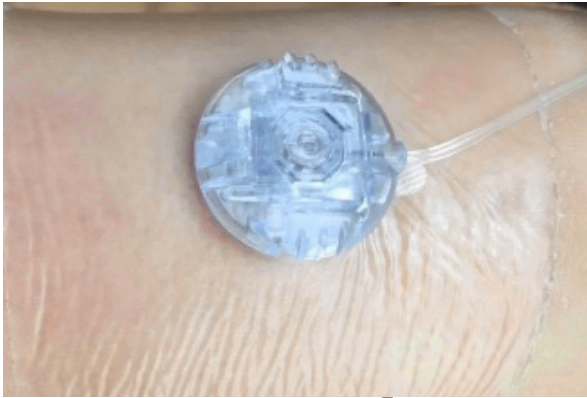
ADVANTAGES:

- Smaller pump
- Decreased risk of bloodstream infections

DISADVANTAGES:

- Site pain can be challenging to manage in some children
- Tape sensitivity
- Sites could become dislodged more easily

Catheter and Infusion Set Options



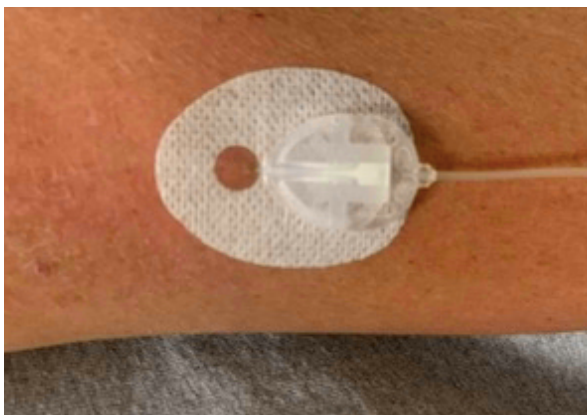
**Cleo®
Catheter**

- All-in-one, single use set with a canister that houses inserter needle and cannula
- Inserted at 90 degrees
- Comes in two sizes, 6 mm and 9 mm
- Needle retracts into the canister after insertion to prevent needle sticks
- Manufactured by Smiths Medical



**MiniMed™
Quick-set™ Catheter**

- Inserted at 90 degrees
- Comes in two sizes, 6 mm and 9 mm
- Requires an introducer for catheter placement that captures the needle
- Manufactured by Medtronic



**MiniMed™
Silhouette™
Catheter**

- Soft cannula infusion set
- Requires an introducer that captures the needle
- Allows for the cannula to be inserted at different angles (20-45 degrees)
- Ideal for thinner body types
- Manufactured by Medtronic

Subcutaneous Site Pain Pearls

Recommended Areas:

- Backs of the upper arms
- Stomach
- Hip area
- Upper buttocks
- Thighs

Avoid these areas:

- Stretch marks
- Scar tissue
- Under clothing waist bands
- Bruises
- Belly folds



I have to manage all this at home? What if there is a problem?

Common Site Issues

- **Help! The treprostinil is leaking!**

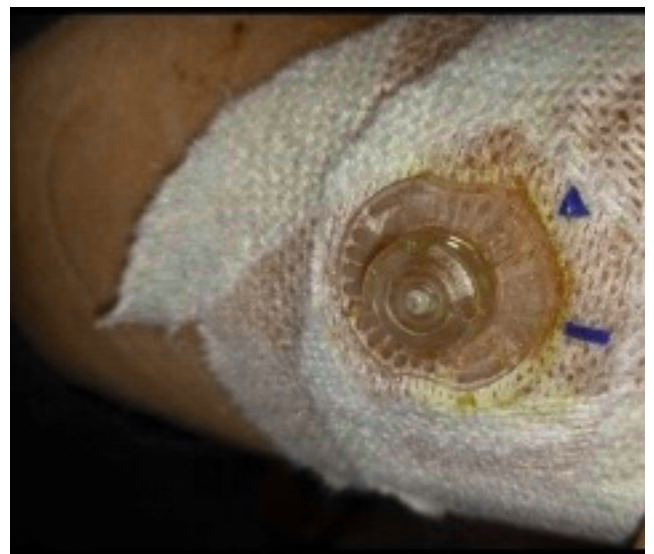
Any leakage of treprostinil requires an immediate site change. A leaking catheter will change the amount of medication being delivered to the child. The child can then experience side effects upon re-initiation of the medication into a new site.

- **What do I do if the catheter breaks?**

On occasion, the catheter can break off of the infusion set and remain dislodged in the tissue. It usually works its way out of the skin on its own. However, it is important to let your healthcare provider know so that the site can be assessed for the need for an intervention.

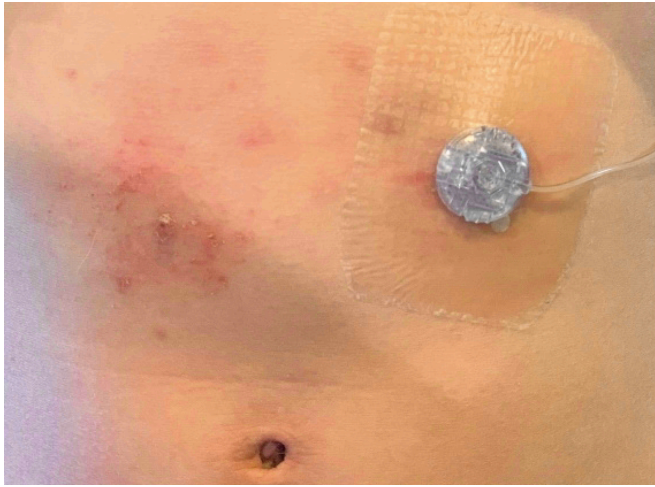
- **This tape is not wanting to stick!**

As time goes on and the catheter remains in place, the adhesive will begin to roll or unstick from the skin. It is necessary to trim the rolled tape and then



reinforce the site with additional tape. On occasion, the tape will fail and the entire site will need to be changed.

Skin Concerns



- **What do I do if my child has a tape sensitivity?**

Many children develop a sensitivity to the type of tape used to secure the site. Your specialty pharmacy and PH team can assist.

Options include alternate clear tape like IV 3000*. Many children report relief with IV 3000* use versus Tegaderm™.

- **I think the treprostinil may have burned my child's skin.**

Treprostinil will burn the skin when leakage occurs. When the treprostinil leaks at the catheter insertion site, you will see a yellow “crust” and smell a strong medicinal odor.

If you feel that your child may have suffered a treprostinil burn, please reach out to your PH team. It may be helpful to take a picture and submit it through your child's online medical portal, if you have that option. Minor burns can be cared for with soap and water. Ice can be helpful for pain. It is important to watch the site for any signs of infection like pus. More severe burns may require the assistance of a wound care specialist.



Hygiene

- **How do I properly bathe my child?**

There are additional measures that must be taken to safely shower. For specific questions, it is always best to consult your PH team. Many children wear waterproof seals to cover their subcutaneous and central venous lines for showers. The key is to ensure that the site and dressings stay clean and dry to prevent infection and/or loss of site.

Activity

- What types of activities can my child participate in?

Some children with pulmonary hypertension are able to play sports and perform physical activities. However, there is always a concern for site dislodgment. Activity restrictions vary from child to child. Talk with your provider about how your child is feeling and what the best plan is for them. If physical activities are difficult for your child, you can keep them involved in other activities such as music, art, or theatre.

School

- How do I navigate school with my child with pulmonary hypertension?

It is helpful that your child's teacher and school administrators understand your child's situation. You should be able to discuss what you need and expect from them. It is also important for them to know what they can expect from you. To help ensure your child's educational needs are met, your child may benefit from an Individualized Educational Program (IEP) or 504 plan. Your hospital may have a school liaison who can assist your navigation within your school system.

Your PH team can work closely with the school to ensure safety. It can be helpful to schedule the specialty pharmacy nurse educator to provide teaching to school nurse(s)/staff. You and your PH team need the school staff to know what to do in case of emergency.

Homebound schooling may be necessary depending on the child's functional limitations. In some circumstances, your PH team and their social worker can help facilitate.

- Should I get my child a medical ID bracelet?

Medical ID bracelets can provide emergency personnel a quick alert of your child's medical needs if you aren't present. It does not need to be lengthy, but could include your child's name, pulmonary hypertension diagnosis, continuous treprostinil running "do not stop pump," and an emergency phone number.



Pain Management & Your Child

An overview of tips & tricks that may be helpful for your child

Every child has a different experience with site pain; some have a little and some have a lot. It is important that you work with your PH team to create an individualized pain management plan for you or your child. It may take some trial and error, but most children and families find a routine that works for them.

EXPECTED SITE REACTIONS INCLUDE REDNESS, INFLAMMATION, AND DISCOMFORT.

PEAK SITE PAIN TYPICALLY OCCURS 2-7 DAYS AFTER STARTING INFUSION THROUGH A NEW SITE

A COMBO OF NON-MEDICINAL APPROACHES, OVER THE COUNTER MEDS, AND PRESCRIPTION MEDS ARE USED TO REDUCE INTENSITY AND DURATION OF PAIN.

The following suggestions come from nurses and providers at eleven PH centers in North America with vast experience caring for subcutaneous treprostinil. These are merely recommendations, though all medical advice should be given by your child's PH provider. Use of these medications is considered by the FDA to be off-label in children. As such, management of these medication should best come from PH centers experienced in PH disease classification and appropriate treatment algorithms.

Treatments for Pain:

By Mouth	
Acetaminophen	Start this on day one of site placement and give every six hours. Alternate with ibuprofen. It is ok to miss this medication during sleep.
Ibuprofen	Start this on day one of site placement and give every six hours. Alternate with acetaminophen. This medication is better tolerated on a full stomach. Consider timing this medication after meals. Motrin will also help with swelling. It is ok to miss this medication during sleep.
Opioids or narcotics like oxycodone	This medication could be considered for severe site pain, which is not controlled by other medications. If you feel that your child needs increased pain control, this medication may be discussed with your PH provider. This medication may cause drowsiness, making it difficult to function.

WHAT I WISH I KNEW: MESSAGES FROM PARENTS

"Be patient. Everyone is different in their pain management. Keep trying new things until you find what works best. It's overwhelming and scary, but it gets better."

"[This will be] manageable. It seems overwhelming at first, but becomes second nature quickly. Take advantage of site changes. It's a great time to take a nice bath or long shower without fear of getting the pump wet. ...it was 100% worth it to switch to SQ Remodulin. It has definitely improved her quality of life."

By Mouth

Neuromodulators like gabapentin

This medication could be considered for severe site pain, which is not controlled by other medications. This should only be used with close monitoring by your child's PH providers. This medication may cause drowsiness, making it difficult to function.

Topical (Applied on Skin)

PLO gel

May be used pre-site placement or help with scarring/nodule breakdown.

Lidocaine Patches

Patches may be cut into strips and placed as a box around the site. These should be used 12 hours on and 12 hours off during periods of peak pain.

Cannabidiol (CBD) Oil

CBD oil has been used with some with success, though bought from reliable stores. Availability may vary from state to state. Use CBD oil at your center's discretion. Please consult your center regarding this use.

Aloe Vera

Aloe vera can soothe the skin.

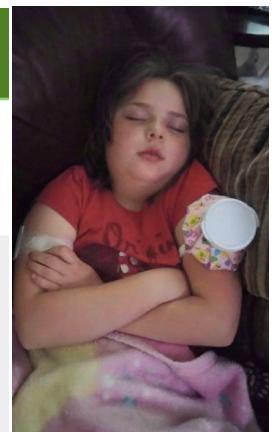
Non-Medication Therapy

Ice

Most find this quite helpful and would use at any onset of pain. Be sure to protect the site that it remains dry.

Heat

Some find heat helpful, but others find that it can increase swelling and redness.



Treatments for Swelling/Itching

Topical (Applied on Skin)	
<p>Fluticasone Spray</p>	<p>Steroid sprays such as fluticasone may be used for new site placement for children who have significant redness, swelling, and pain associated with new sites. Many centers feel that this does not have a strong effect, but works for some children.</p>
<p>Hydrocortisone cream or ointment</p>	<p>Steroid creams or ointment may help with itching related to new site placement. Be careful with the integrity of the site dressing when placing the cream or ointment.</p>
<p>Diphenhydramine cream</p>	<p>Antihistamine creams may help with itching associated with new site placement. Be careful of the integrity of the site dressing when placing the cream or ointment.</p>
<p>By Mouth</p>	
<p>H1/H2 Blockers</p>	<p>Consider H1 blocker like cetirizine and/or H2 blocker (like famotidine) on the starting day of dry/new site placement through day 7 of new site or as ongoing therapy. Consult with your PH provider to determine the most appropriate dosing for your child.</p>
<p>Steroids</p>	<p>Oral systemic steroids could be used for significant site swelling. Consult your PH provider if this is occurring.</p>



By Mouth

Diphenhydramine

An antihistamine such as diphenhydramine may be used for itchiness or swelling of a new site. This medication may make your child drowsy. In some children, it has the opposite effect and can make them agitated. Consult your PH provider for the most appropriate dosing for your child.

Non-medication Therapy

Compression sleeve/wrap i.e. Ace™ bandage, Coban™ wrap

Compression around the site may relieve discomfort related to swelling associated with new site placement. It may also help to minimize dislodgment.



Example Pain Schedule for New Site Placement

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Ice/Heat	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day
Cetirizine or Loratadine	1x/day	1x/day	1x/day	1x/day	1x/day	1x/day	1x/day	1x/day	1x/day	1x/day
Famotidine	2x/day	2x/day	2x/day	2x/day	2x/day	2x/day	2x/day	2x/day	2x/day	2x/day
Diphenhydramine	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed
Ibuprofen	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours
Acetaminophen	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours	Every 6 hours

* If prescribed by your PH provider

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
*Lidocaine Patch	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off	12 hours on/ 12 hours off
*PLO gel	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day	3-4x/day
*Gabapentin	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)	3x/day (lowest dose)
*Oxycodone	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed

Additional Tips:

1. Plan ahead: place a “dry site” if you think your site will need changing in the next couple of days. Wait 24 hours (if possible) before hooking the new site up to your pump.
2. Be choosy: pick your new site location when you are sitting up to avoid placing on the folds of your belly or at the waistband of your pants
3. Do not move the site unless a quiet site starts to drain, becomes sore, becomes hard, or you notice a sudden change in your PH symptoms. Sites may be safely left in place for weeks and months.
4. Do not change a site because of redness. Redness is only worrisome when accompanied by other symptoms.
5. Do not change the dressing covering your site. This may lead to accidentally pulling out your site.
6. When the dressing around your site begins to peel away, cut the excess dressing and place new dressing on top. You could also use a skin barrier wipe to reinforce the dressing.
7. Create a stress/dependent loop with tubing to prevent the site from being dislodged.
8. Thread tubing under your shirt and tuck your pump in your bra, fanny pack or pocket during the day.



9. Consider placing a compression wrap over an arm or leg site to help protect the site.
10. Keep the site as dry as possible.

Parent Resources

Resource	Website Link
Pediatric Pulmonary Hypertension Network	www.pphnet.org
Pulmonary Hypertension Association	www.phassociation.org
Your local PHA support group	https://phassociation.org/support/
Your Child's PH Provider and Team	



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