



Prostacyclin Therapies for WHO Group 1 PH (PAH): Pills, Pumps and Other Devices

2018 PHA on the Road – Long Beach, Calif.

Session Description

Panelists will discuss the seven medications that target the prostacyclin pathway for WHO Group 1 PH (PAH). Discussion will focus on medication properties and administration, choosing the right therapy, the general management of side effects and the newest developments in administration techniques, including mixing with special diluents, miniature devices and the implanted treprostinil pump. The patient experience will also be discussed during this session.

Learning Objectives

At the end of the session attendees will be able to:

- Learn about new developments in infused prostacyclin therapies.
- Gain an understanding of the common side effects of prostacyclin therapies.
- Gain tips on how you and your health care team can discuss what therapy is right for you.

Overview of FDA-Approved Prostacyclin Therapies for PAH

- Prostacyclin and its biologic effects
 - Acts on the prostacyclin pathway, can be used alone or in combination with medications from the other two pathways (endothelin and nitric oxide).
 - Prostacyclin is naturally occurring, produced by the inner lining of the lung blood vessels (endothelium).
 - Properties: vasodilates (opens blood vessels), inhibits platelet aggregation (prevents platelet clumping) and anti-smooth muscle proliferation (slows the growth of the smooth muscle layer of the vessels).
- Synthetic prostacyclins/prostacyclin analogues:
 - Epoprostenol (Flolan® and Veletri®) – Intravenous.
 - Treprostinil (Remodulin®) – Intravenous or subcutaneous.
 - Iloprost (Ventavis®) – Inhaled, six to nine times per day.
 - Treprostinil (Tyvaso®) – Inhaled, four times per day.
 - Treprostinil (Orenitram®) – Oral, two or three times per day.
 - Prostacyclin receptor agonist – Selexipag (Uptravi®) - Oral, two times per day.

New Developments in Infused Prostacyclin Therapies

- Implantable Treprostinil (Remodulin®) – Implantable pump was recently approved by the Food and Drug Administration (FDA); anticipated availability in 2019.
- Trevyent™ – Treprostinil patch pump is in development.
- pH 12 diluent for Flolan – store in fridge up to eight days, administer at room temp (up to 95°).

Common Side Effects of Prostacyclin Therapies

- Side effects are highly variable from person to person, but most can be managed.
- Side effects may occur at start of therapy and with up-titration (increasing the dose).



Prostacyclin Therapies for WHO Group 1 PH (PAH): Pills, Pumps and Other Devices

2018 PHA on the Road – Long Beach, Calif.

- Management of side effects may require temporarily reducing the dose or slowing the up-titration until they are tolerable; **talk to your PH team before reducing your PAH-specific therapies.**
- Potential acute side effects may include hypotension (low blood pressure), nausea, flushing, headache, diarrhea, jaw pain, leg/back pain.
- Potential chronic side effects may include flushing, headache, diarrhea, jaw pain, leg/back pain, thrombocytopenia (decrease in platelet count), increased risk of bleeding.
- Other side effects related to the route of medication administration may include the following:
 - Oral: More pronounced GI side effects such as nausea and diarrhea.
 - Inhaled: Cough is the most common side effect can be lessened in several ways; fewer patients experience systemic side effects.
 - Subcutaneous: Site reaction is highly variable, with multiple ways to treat (technique, topical and/or oral medications) and treatments are time limited.
 - Intravenous: Blood stream infection – must use a careful technique and carefully choose the correct diluent.
- Side effects often get better over time and the improvement of PAH symptoms often outweighs the negative side effects of PH medications.

Selecting the Right Therapy for You

- Different forms and routes of medication administration offer many choices for healthcare providers and patients.
- Choosing the right medication depends on the severity of disease, goals for treatment, lifestyle considerations and available support:
 - Oral prostacyclin therapies are like "a pump in a pill" dose and frequency must be exact.
 - With inhaled therapies, the best results are seen in patients when taken at the prescribed frequency, but you must take the device with you when you leave the house.
 - In infused prostacyclin therapies:
 - A back-up caregiver is preferred in case of emergencies.
 - The short half-life of epoprostenol (Flolan® and Veletri®) require immediate medical attention if the infusion is interrupted for any reason.
 - Attention to detail and manual dexterity are required to mix medication properly.
 - Vigilance and hygienic cleanliness must be maintained to prevent infusion line infection.