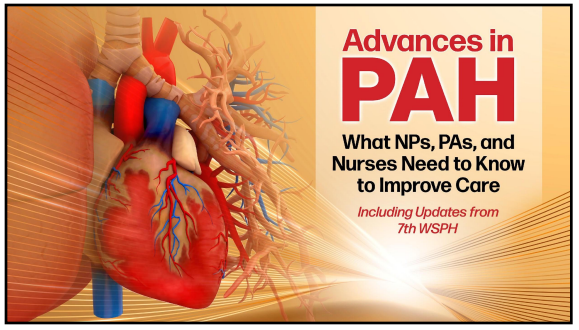
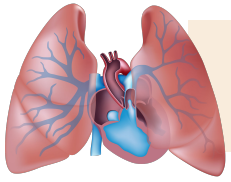


Learning Objectives

- Identify the updated diagnostic criteria and classification of PAH.
- Plan effective care for patients with PAH that considers the side effect profile, method of dosing and administration, adverse events, and disparities.
- Summarize updated treatment pathways and therapeutic targets in the management of PAH.

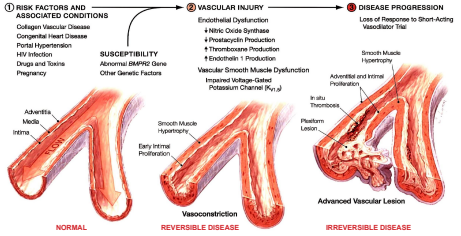
Hemodynamic Definition of PAH



- mPAP > 20 mmHg at rest
- PAWP ≤ 15 mmHg
- PVR > 2 Wood units

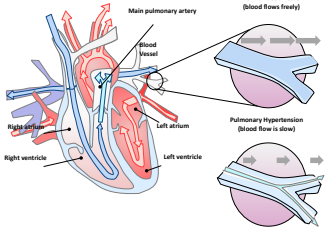
McLaughlin VV et al. *Circulation*. 2009; 119:2250-2294.
Hoeper MM et al. *J Am Coll Cardiol*. 2013; 62 (25 Suppl):D42-D50.
Simonneau G, et al. *Eur Respir J*. 2019;53(1):1801913.
Humbert M, et al. *Eur Heart J*. 2023;Apr 17:44(15):1312.

Pathophysiology



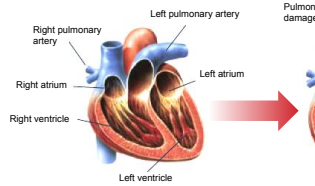
Gaine S. *JAMA*. 2000;284(24):3160-3168.

Pathophysiology



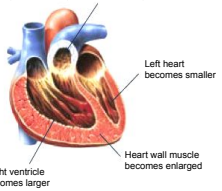
PH is a Disease of the Pulmonary Arteries Leading to Right Heart Abnormalities

NORMAL HEART



PULMONARY HYPERTENSION

Pulmonary artery wall and its smaller vessels become damaged, restricting blood flow to lungs



1. Farber H, Loscalzo J. Pulmonary arterial hypertension. *N Engl J Med*. 2004;351:1655-1665
2. http://www.nhlbi.gov/health/dci/Diseases/pah/pah_what.html. Accessed March 22, 2018
3. Gaine S, Rubin LJ. Primary pulmonary hypertension. *Lancet*. 1998;352:719-725

Updated Diagnostic Algorithm

UPDATE FROM 7th WORLD SYMPOSIUM

Diagnosis and treatment of alternative condition (mostly heart or lung disease)
Referral of patients with suspected PH-ILD or severe PH associated with other chronic lung diseases or severe cpcPH to PH centre

STEP 1	STEP 2	STEP 3	STEP 4	PH CENTRE STEP 5
Medical history (risk conditions), **symptoms** (WHO-FC), **signs of PH**	**Simple noninvasive tools** (chest radiography, ECG, basic laboratory testing including BNP/NT-proBNP, oxygen saturation)	**Echocardiography** (TRV, 2D and Doppler indices of PH/#, left heart assessment + **Airway and lung assessment** (ABG, PFT, DLCO, imaging (preferably chest CT; P/G/ONO)	***V'/Q'* scan** + Detailed laboratory testing + **Additional testing** (6MWT, ± CPET, ± cardiac MRI)	**RHC** with vasoreactivity testing/exercise testing/fluid loading (as needed) and comprehensive PH workup

Fast-track referral for patients with high probability of PAH/CTEPH or high urgency

Kovacs G, et al. *Eur Respir J*. Published online August 29, 2024. doi:10.1183/13993003.01324-2024

Diagnosis of PAH Requires Right Heart Catheterization

Right Heart Catheterization

- Confirm diagnosis
- Excludes other etiologies of PH
  - Intracardiac or extracardiac shunts
  - Left-heart-disease
- Measures degree of right-heart dysfunction
  - Right atrial pressure
  - Cardiac output

Essential Components Of Invasive Hemodynamic Assessment

- O_2 Saturations
- RAP
- PCWP, or LVEDP
- Cardiac output/cardiac index
- Pulmonary vascular resistance
- Vasodilator challenge for : idiopathic, heritable, and PAH associated with drugs and toxins.

McGoon M, et al. *Chest*. 2004; 126:14S-34S.
McLaughlin VV, et al. *J Am Coll Cardiol*. 2009; 53:1573-1619.
Galiè N, et al. *Eur Respir J*. 2019 Jan 24;53(1).

7th World Symposium Updates to Group 1 and 2 PH Classification

UPDATE FROM 7th WORLD SYMPOSIUM

Group 1: PAH

- **1.1 Long-term responders to calcium channel blockers**
- 1.2 Heritable
- **1.3 Associated with drugs and toxins**
- 1.4 Associated with:
  - 1.4.1 connective tissue disease
  - 1.4.2 HIV infection
  - 1.4.3 portal hypertension
  - 1.4.4 congenital heart disease
  - 1.4.5 schistosomiasis
- 1.5 PAH with features of venous/capillary (PVOD/PCH) involvement
- 1.6 Persistent PH of the newborn

Group 2: PH associated with left heart disease

- 2.1 Heart failure:
  - 2.1.1 with preserved ejection fraction
  - 2.1.2 with reduced or **mildly reduced ejection fraction**
  - 2.1.3 **cardiomyopathies with specific etiologies**
- 2.2 Valvular heart disease:
  - **2.2.1 aortic valve disease**
  - **2.2.2 mitral valve disease**
  - **2.2.3 mixed valvular disease**

Kovacs, Bartolome, Denton, et all Definition, classification and diagnosis of pulmonary hypertension. *Eur Respir J* 2024

Updates to Drugs and Toxins DT-PH

- **Added to definite:**
  - Mitomycin-C and carfilzomib
- **Added to possible:**
  - Other alkylating agents
  - Bevacizumab
  - Bortezomib
  - Suggest replacing indirubin (Chinese herb Qing-Dai) with indigo naturalis (Chinese herb Qing-Dai) as possibly being associated with PAH

Drugs and toxins associated with pulmonary arterial hypertension (PAH)

Definite association	Possible association	
Aminorex	Alkylating agents	Indigo naturalis (Chinese herb Qing-Dai)
Benfluorex	Amphetamines	Interferon-α and –β
Carfilzomib	Bevacizumab	Leflunomide
Dasatinib	Bortezomib	L-tryptophan
Dexfenfluramine	Bosutinib	Phenylpropanolamine
Fenfluramine	Cocaine	Ponatinib
Methamphetamines	Diazoxide	Solvents (trichloroethylene)[a]
Mitomycin C[a]	Direct-acting antiviral agents against hepatitis C virus (sofosbuvir)	St John's wort
Toxic rapeseed oil		

[a]PA with features of venous (pulmonary veno-occlusive disease)/capillary (pulmonary capillary haemangiomatosis) involvement.

Kovacs G, et al. *Eur Respir J*. Published online August 29, 2024. doi:10.1183/13993003.01324-2024

7th World Symposium Updates to Groups 3-5

UPDATE FROM 7th WORLD SYMPOSIUM

Group 3: PH associated with lung diseases and/or hypoxia

- **3.1 COPD and/or emphysema**
- **3.2 Interstitial lung disease**
- **3.3 Combined pulmonary fibrosis and emphysema**
- 3.4 Other parenchymal lung diseases
- **3.5 Nonparenchymal restrictive diseases**:
  - 3.5.1 hypoventilation syndromes
  - 3.5.2 **pneumonectomy**
  - 3.6 Hypoxia without lung disease (eg high altitude)
  - 3.7 Developmental lung diseases

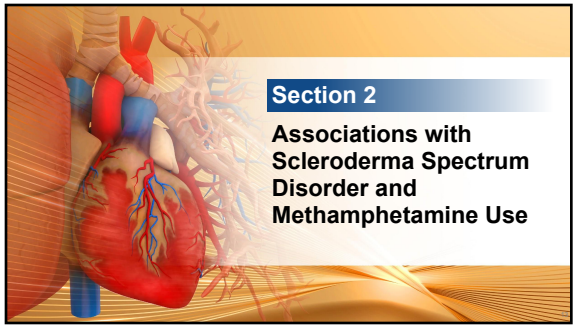
Group 4: PH associated pulmonary artery obstructions

- 4.1 Chronic thromboembolic PH
- 4.2 Other pulmonary artery obstructions

Group 5: PH with unclear and/or multifactorial mechanisms

- 5.1 Hematologic disorders
- 5.2 Systemic disorders: **sarcoidosis, pulmonary Langerhans cell histiocytosis and neurofibromatosis type 1**
- 5.3 Metabolic disorders
- 5.4 Chronic renal failure with or without haemodialysis
- 5.5 Pulmonary tumour thrombotic microangiopathy
- 5.6 Fibrosing mediastinitis
- **5.7 Complex congenital heart disease**

Kovacs, Bartolome, Denton, et all Definition, classification and diagnosis of pulmonary hypertension. *Eur Respir J* 2024



Section 2

Associations with Scleroderma Spectrum Disorder and Methamphetamine Use

DETECT Algorithm for Early Identification of CTD-PH

STEP 1

Non-Echocardiographic Data (6 Variables)

Non-Echo Variables:
- FVC % predicted/DLCO % predicted
- Current/past telangiectasias
- Serum ACA
- Serum NT-proBNP
- Serum urate
- ECG/right axis deviation

Total Points >300

NO

No Echocardiography

STEP 2

Echocardiographic Data

Step 1 Points + Echo Variables
- Right atrium area
- TR velocity

Total Points >35?

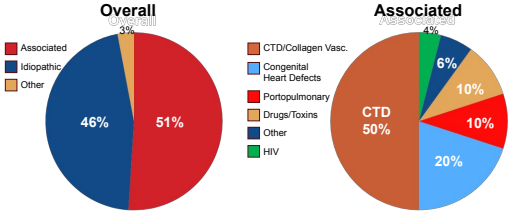
NO — **No RHC**

YES — **If echo evidence of PH, patients are referred for RHC**

Coghlan JG, et al. *Ann Rheum Dis*. 2014;73(7):1340-1349.

14

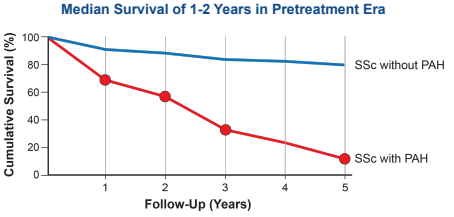
Nearly 25% of PAH is CTD Related



Based on Venice Clinical Classification (2003); 2,967 patients.
Adapted from Badesch DB, et al. *Chest*. 2010;137(2):376-387.

15

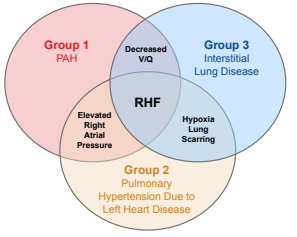
Survival in SSc With and Without PH



Adapted from Steen V, Medsger TA Jr. *Arthritis Rheum*. 2003;48(2):516-522.

16

Patients With CTD Can Also Have Group 2, 3 PH



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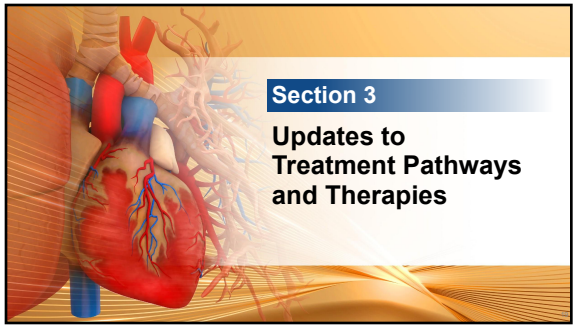
Methamphetamine Associated PAH

- Urine drug screening:
  idiopathic and history of substance use disorder
- Routes of use: (Meth)amphetamine—
  inhaled, smoked, snorted, orally ingested, injected
- Cardiovascular toxicity :

Kovacs G, et al. Updated ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J*. 2024.

18



Section 3

Updates to Treatment Pathways and Therapies

Goals of Therapy

UPDATE FROM 7th WORLD SYMPOSIUM

Domain	Treatment goals
Exercise tolerance	6MWD >440 m WHO-FC I or II
RV function and strain	BNP <50 ng·L^{-1} NT-proBNP <300 ng·L^{-1}
Hemodynamics	RAP <8 mmHg; CI ≥2.5 L·min^{-1}·m^{-2}; SVI >37 mL·m^{-2}; S_{vo2} >65%; PVR <5 WU

RV: right ventricle; 6MWD: 6-min walk distance; WHO-FC: World Health Organization functional class; BNP: brain natriuretic peptide; NT-pro BNP: N-terminal pro-BNP; RA: right atrium; TR: tricuspid regurgitation; TAPSE/sPAP: tricuspidannular plane systolic excursion/systolic pulmonary artery pressure ratio (estimated by echocardiography); RAP: right arterial pressure; CI: cardiac index; SVI: stroke volume index; S_{vo2}: mixed venous oxygen saturation; PVR: pulmonary vascular resistance; WU: Wood Units; mPAP: mean pulmonary artery pressure; PAC: pulmonary arterial compliance; ESC: European Society of Cardiology; ERS: European Respiratory Society.
Dardi F, et al. *Eur Respir J*. Published online August 29, 2024. doi:10.1183/13993003.01323-2024

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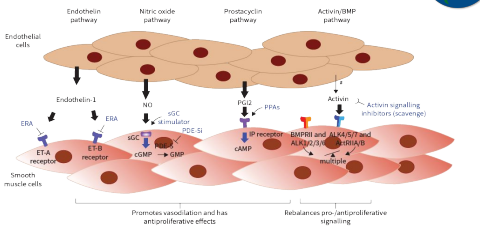
There Are Now 4 Treatment Pathways for PAH

UPDATE FROM 7th WORLD SYMPOSIUM



Chin KM, et al. *Eur Respir J*. Published online August 29, 2024. doi:10.1183/13993003.01325-2024

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Route of Administration of FDA-Approved PAH-Specific Therapies

Pathway	Class	Name	Route of Administration		
			Oral	Inhaled	IV/SC
Endothelin pathway	ERA	Ambrisentan	Y		
		Bosentan	Y		
		Macitentan	Y		
Combination			ERA + PDE5i		Macitentan + Tadalafil
Nitric oxide pathway			PDE5i		Sildenafil
					Tadalafil
			sGCS		Riociguat
Prostacyclin pathway	PRA	Selexipag	Y		IV
	PA	Epoprostenol			IV
		Ulotepla inhaled		Y	
		Treprostinil	Y	Y	IV and SC
Activin signalling pathway	ASI	Sotatercept			SC

ASI, activin signaling inhibitor; ERA, endothelin receptor antagonist; FDA, Food and Drug Administration; PA, prostacyclin analog; PDE5i, phosphodiesterase type 5 inhibitor; PRA, prostacyclin receptor agonist; SGCS, soluble guanylate cyclase stimulator.
Sahay S, et al. *Am J Respir Crit Care Med*. 2024;210(5):581-592.

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Treatment Algorithm

UPDATE FROM 7th WORLD SYMPOSIUM

Therapy for group 1 PAH including IPAH, HPAH, DT-PAH and CTD-PAH[a]

Initial risk assessment[b]

Not high risk[c]
Combination ERA + PDE-5i

High risk[c,f]
Combination iv/sc PPA, ERA, PDE-5i

First follow-up risk reassessment at 3–4 months and repeated frequently

Low risk[d]
Continue initial therapy

Intermediate-low risk[d]
Add activin-signaling inhibitor, oral or inhaled PPA
Can consider switch PDE-5i to sGCS

Intermediate-high risk[d]
Add iv/sc PPA or activin-signaling inhibitor

High risk[d]
Add iv/sc PPA (1st choice if not on) or activin-signaling inhibitor

Persistent intermediate-high or high
Maximal Rx: 4-drug iv/sc PPA, ERA, PDE-5i or sGCS, activin-signaling inhibitor
Lung transplant evaluation

Treatment Algorithm Key Points

a. The treatment algorithm is intended for patients with confirmed group 1 PAH (phenotypically clear-cut, including **mPAP ≥25 mmHg and PVR >3 Wood Units** and no significant response on acute vasoreactivity testing). See text for treatment in PAH with complex phenotypes.
b. **Risk assessment** should be performed at baseline, within 3–4 months and periodically thereafter, and using FC, 6MWD and natriuretic peptides as part of a validated risk calculator. Haemodynamics, RV imaging and other measures should be used to supplement risk assessment.
c. **Initial triple therapy** with an iv/sc PPA is recommended in high-risk patients and may be considered in non-high risk with severe hemodynamics and/or poor RV function.
d. Most **low-risk patients** at follow-up should continue initial therapy.
e. Clinical trials with oral and inhaled treprostinil included **only patients on monotherapy**, while studies of selexipag and sotatercept included patients on combination therapy.
f. **Transplant referral** should be considered for select high-risk patients at diagnosis, and for intermediate-high and high-risk patients at first or subsequent follow-up.

PAH: pulmonary arterial hypertension; IPAH: idiopathic PAH; HPAH: hereditary PAH; DT: drug and toxin; CTD: connective tissue disease; ERA: endothelin-1 receptor antagonist; PDE-5i: phosphodiesterase-5 inhibitor; iv: intravenous; sc: subcutaneous; PPA: prostacyclin pathway agent; sGCS: soluble guanylyl cyclase stimulator; Rx: prescription; mPAP: mean pulmonary artery pressure; PVR: pulmonary vascular resistance; FC: functional class; 6MWD: 6-min walk distance; RV: right ventricle.
Chin KM, et al. *Eur Respir J*. Published online August 29, 2024. doi:10.1183/13993003.01325-2024

23

Endothelin Receptor Antagonists (ERAs)

Drug	Route of Administration	Comment
Bosentan	Oral, BID	Monitor LFTs monthly; monthly pregnancy testing for all females of child-bearing status; Risk Evaluation and Mitigation Strategy -needs specialty pharmacy
Macitentan	Oral, QD	Monthly pregnancy testing for all females of child-bearing status; (REMS is optional as of April 2025); needs specialty pharmacy
Ambrisentan	Oral, QD	Monthly pregnancy testing for all females of child-bearing status as clinically indicated; (REMS is optional as of April 2025); needs specialty pharmacy

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Phosphodiesterase-5 (PDE-5) Inhibitors and Guanylate Cyclase Stimulators (sGC)

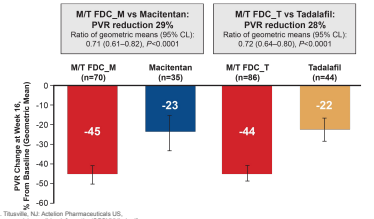
Drug	Route of Administration	Comment
Sildenafil	Oral, TID	Not be used with nitrates or guanylate cyclase stimulator
Tadalafil	Oral, QD	Not be used with nitrates or guanylate cyclase stimulator
Riociguat	Oral, TID	Not be used with nitrates and/or phosphodiesterase 5 inhibitors (PDE-5Is); SP for embryo toxicity; requires nursing visit for titration and monthly pregnancy testing

Barst RJ. *Vasc Health Risk Manag*. 2007;3:11-22.
SP = Requires specialty pharmacy (SP) where medication is delivered to home monthly.

New Therapy: Fixed-Dose Combination of Tadalafil and Macitentan

A DUE Phase 3 Trial of Fixed-Dose Combination (N=187)

- M/T FDC combines macitentan 10 mg/day + tadalafil 40/day
- Significant improvement in PVR with combination vs monotherapy after 15 weeks
- Recently approved FDC tablet could improve adherence and simplify treatment



OPSYNVI (macitentan and tadalafil) [Prescribing Information]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.;https://www.jansenlabels.com/package-insert/product-monograph/prescribing-information/OPSYNVI-pi.pdf

Chin K, et al. ACC 2023. Session 409-15.

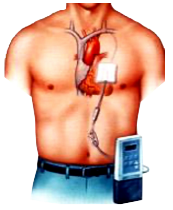
Prostacyclin Pathway Meds

Drug	Route of Administration
Epoprostenol	Continuous IV infusion
Treprostinil	Continuous IV infusion Continuous SC infusion Inhalation Oral, BID or TID
Yutrepia	Inhaled QID
Selexipag	Oral BID IV BID

NOTE: All IV Prostanoids require a dedicated [illegible] [illegible]
NS, normal saline (0.9%); SWFI, sterile water for injection.

Epoprostenol

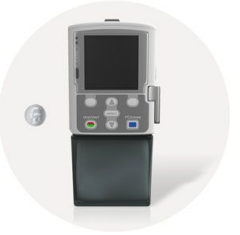
- 1st FDA approved drug for PAH
- Gold standard for high-risk patients
- Continuous IV infusion via a central venous catheter
- 3- to 6-minute half-life
- Two brands: Flolan® and Veletri®
- Once daily mixing—powder and diluent
- Provided by specialty pharmacies and requires home teaching



Flolan prescribing information. Available: https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/020444s021lbl.pdf. Accessed: August 11, 2020.

IV Treprostinil and Epoprostinil Pump

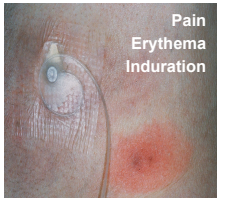
CADD®-SOLIS AMBULATORY INFUSION PUMP



CADD®-SOLIS is a registered trademark of Smiths Medical System.

Treprostinil (Remodulin®) SQ

- Infusion site pain & site reaction
  - Most common for 5-7 days after site change
- Varies from:
  - Patient to patient
  - Site to site
- Generally, not dose-limiting
- 82% experience site pain
  - Only 7% stop therapy



RemunityPro Pump

A programmable remote control is part of the s

Not shown at actual size or scale.

Remodulin [package insert]. Research Triangle Park, NC: United Therapeutics Corporation; 2023. 2. Remunity User Guide. Research Triangle Park, NC: United Therapeutics Corporation; 2023

Inhaled Treprostinil

- 2 formulations: Tyvaso Inhalation System or DPI
- Dosed QID and up-titrated
- Approved for Group 1 and Group 3 PH
- AEs: headache, diarrhea, nausea and cough, headache, nausea, dizziness, flushing, throat irritation
- Also improved for ILD-PH: INCREASE study

Tyvaso prescribing information. Available: https://www.tyvaso.com/hcp/pdf/Tyvaso-PI.pdf?v=1020. Accessed: September 8, 2020.

YUTREPIA Inhalation Powder

Print technology for uniform particle size and deep lung deposition

Low inspiratory effort device

Nebulized Treprostinil Breaths	YUTREPIA™ QID Dose (mcg)	YUTREPIA™ Capsule Combination
≤5	26.5	26.5 mcg per capsule
≥6	53	53 mcg per capsule
≥9	79.5	79.5 mcg per capsule
≥12	106	106 mcg per capsule
≥15	132.5	53 mcg + 79.5 mcg per capsule
≥18	159	79.5 mcg + 79.5 mcg per capsule
≥21	185.5	79.5 mcg + 106 mcg per capsule
≥24	212	106 mcg + 106 mcg per capsule

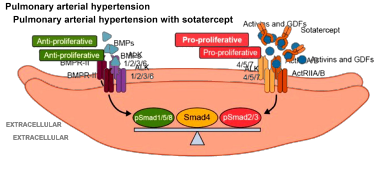
Selexipag

- Oral/IV Selective IP receptor agonist
- Oral Dosing starts at 200mcg BID and increased weekly by 200mcg BID to highest tolerated dose or 1600mcg BID
- Similar side effects to IV prostacyclin but less severe
- IV Dose: BID at a dose that corresponds to the patient's current dose of tablets as an 80-minute intravenous infusion
  - Used when hospitalized and unable to take oral formulation

UPTRAVI® (selexipag) full Prescribing Information. Actelion Pharmaceuticals US, Inc

New Therapy: ASI pathway—Sotatercept

PAH is a progressive disease driven by pulmonary vascular remodeling due in part to an imbalance in anti-proliferative (BMPR-II-mediated) and pro-proliferative (ActRIIA-mediated) signaling pathways, resulting in hyperproliferation of vessel wall cells.

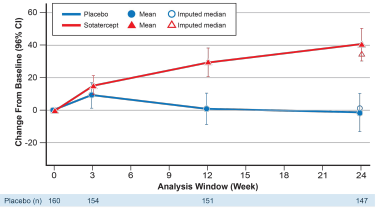


Sotatercept is proposed to act as a reverse-remodeling agent, to rebalance the anti-proliferative and pro-proliferative signaling.

STELLAR Clinical Trial: Sotatercept

Primary Endpoint : change in 6MWT : 40 meters in treated group -1 in placebo group

Met primary endpoint and 8 of 9 secondary endpoints



Placebo (n)	160	154	151	147
Sotatercept (n)	163	157	154	157

Phase 3 Trial of Sotatercept for Treatment of Pulmonary Arterial Hypertension. Badesh, et al. NEJM 2023

DOI: 10.1056/NEJMoa2213558

Overall Summary of Adverse Events of Interest

Note: pericarditis recently added

	Placebo (N=160) n (%)	Sotatercept (N=163)n (%)
TEAEs of interest or special interest	72 (45.0)	97 (59.5)
Bleeding events	25 (15.6)	52 (31.9)
Telangiectasia	6 (3.8)	23 (14.1)
Increased hemoglobin (increased hematocrit, increased RBC)	0	10 (6.1)
Thrombocytopenia	5 (3.1)	14 (8.6)
Increased blood pressure	1 (0.6)	7 (4.3)
TEAEs with incidence ≥10% in one or more treatment groups		
Epistaxis	3 (1.9)	33 (20.2)
Telangiectasia	6 (3.8)	23 (14.1)

Cumulative results through data cut-off date

Supportive Therapies

- Anticoagulation
- Supplemental oxygen therapy
- Diuretics
- Physical activity/supervised rehabilitation
- Pregnancy prevention/contraception
- Psychological support
- Palliative care

Grünig E, Benjamin N, Krüger U, et al. General measures and supportive therapy for pulmonary arterial hypertension: Updated recommendations from the Cologne Consensus Conference 2018. *Int J Cardiol*. 2018;272S:30-36.

Lung Transplantation for PAH

- Patients with PAH receive double lung transplant
- Previously epoprostenol (Flolan®) was a "Bridge to Transplantation"
- Now reserved for those patients who fail maximum medical therapy
- Survival is 5-7 years on average after bilateral lung transplantation
- From 7th World Symposium: Patients should be referred for transplant evaluation when they remain intermediate-high or high risk

Klinger R, et al. *Chest*. 2019;155(3):565-586. Available: https://journal.chestnet.org/article/S0012-3692(19)30002-9/fulltext. Accessed: August 12, 2020.
Frost A, et al. *Eur Respir J*. 2019 Jan 24:53(1).

Emerging Treatments in Ongoing Trials

Drug Name*	Mechanism	Route	Trial Name (ID Number)	Trial Phase	Study Completion
MK-5474	sGC stimulant	INH	INSIGNIA-PAH (NCT04732221)	3	Jan 2028
Ralinepag	PRA	Oral	ADVANCE OUTCOMES (NCT03626688)	3	Dec 2025
Seralutinib	PDGFR antagonist	INH	PROSPERA (NCT04816604)	3	2026
Macitentan 75mg	ERA	Oral	UNISUS (NCT04273945)	3	2029

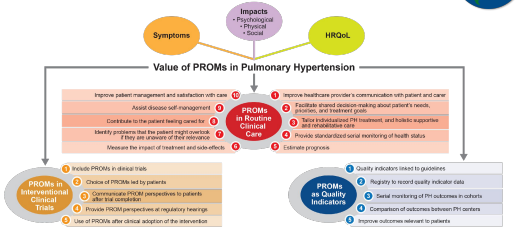
OPSUMIT (macitentan) [Prescribing Information]. Titusville, NJ: Actelion Pharmaceuticals US, Inc. https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/OPSUMIT-pi.pdf

Section 4

Disparities in Care and Patient Perspective

Patient-Related Outcome Measures (PROMS)

UPDATE FROM 7th WORLD SYMPOSIUM



Ford HJ, et al. *Eur Respir J*. Published online August 29, 2024. doi:10.1183/13993003.01129-2024

Disparities in PH Care

- In a small, single-center, retrospective cohort, non-white patients with PAH had worse outcomes than white patients with PAH.
- In two studies using national registries of death certificate data, African American (AA) women had the highest mortality rates among patients with PAH. Aug 28, 2017
- Lower socioeconomic status is associated with worse outcomes in pulmonary arterial hypertension

1. Al-Naamani N, Paulus JK, Roberts KE, Pauculo MW, Lutz K, Nichols WC, Kawut SM. Racial and ethnic differences in pulmonary arterial hypertension. *Pulm Circ.* 2017 Oct-Dec;7(4):793-796. doi: 10.1177/2045893217732213. Epub 2017 Sep 15. PMID: 28849992; PMCID: PMC5703127.
2. Wu W-H, Yang L, Peng F-H, Yao J, Zou L-L, Liu D, Jiang X, Li J, Gao L, Qu J-M, et al. Lower socioeconomic status is associated with worse outcomes in pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2013;187:303–310.

Update from 7th World Symposium: Disparities

UPDATE FROM 7th WORLD SYMPOSIUM

Comments From Patient Taskforce International Members:

"In terms of available treatments, we are well behind America and Europe. This limits options for patients".

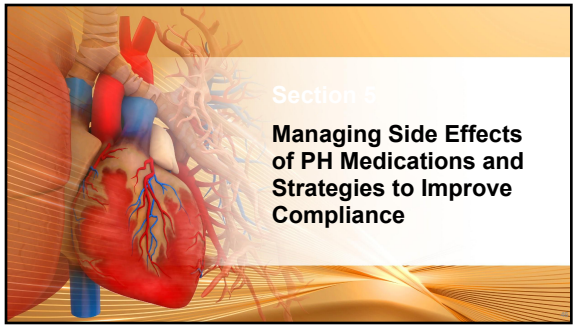
"State patients cannot get many of the PH medications, whereas some private patients have access depending on their medical insurance scheme. State patients' access is limited and have to have generic where available".

"I have never used insurance or national healthcare scheme to pay for my medication, always out of pocket. From my knowledge and experience, I haven't found any insurer that is willing to cover my medications".

https://doi.org/10.1183/13993003.01129-2024 2
European Respiratory Journal
7th World Symposium On Pulmonary Hypertension | H.J. Ford Et Al.

Shared Decision-Making (SDM)

- Shared decision making
  - Allows patients to participate actively in their treatment plans
  - Enhances treatment adherence
  - Improves patient satisfaction and outcomes
  - Allows patients to make better choices that reflect their personal goals, i.e pursuing aggressive therapies or prioritizing quality of life
- Implementing SDM requires
  - Clear and comprehensive communication between healthcare providers and patients
  - Providers to present complex information in a way that is easy to understand
- Despite its benefits, SDM is not consistently applied in clinical practice due to
  - Barriers such as time constraints
  - Varying levels of patient health literacy posing significant challenges



Section 6

Managing Side Effects of PH Medications and Strategies to Improve Compliance

Endothelin Receptor Antagonists: Side Effects

- Nasal congestion
- Abnormal hepatic function*
  - Monthly LFTs required for bosentan
- Anemia
  - Monitor CBC quarterly
  - LFT elevation with bosentan
- Edema
  - Lower extremity edema may require diuretic adjustment
- Teratogenic
  - Use requires dual contraceptive methods (hormonal plus barrier)

***PHA Scientific Leadership Council recommends LFT testing at onset of all treatments for PAH and periodically thereafter, at prescriber's discretion.**

PHA , Understanding the side effects of pulmonary hypertension medicatioln, Gillian Leung, PharmD, BCCP; Yash Kothari, M.D 2023.

PDE-5: Side Effects

- Nosebleed
- Headache
- Dyspepsia
- Flushing
- Diarrhea
- Visual changes

Most side effects can be managed with acetaminophen and anti-diarrhea meds

Contraindicated with use of nitrate

PHA , Understanding the side effects of pulmonary hypertension medicatioln, Gillian Leung, PharmD, BCCP; Yash Kothari, M.D 2023.

sGC Stimulator: Side Effect

- Headache
- Dizziness
- Dyspepsia/gastritis
- Nausea
- Diarrhea
- Hypotension– may need to lower dose (rarely)
- Vomiting– anti-emetics
- Anemia– monitor
- Gastroesophageal reflux–

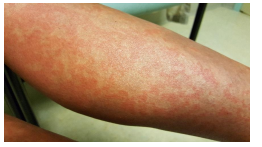
Contraindicated in pregnancy and with the use of nitrates in any form, or with use of PDE inhibitors

Pharmacologic therapy of pulmonary hypertension medication. Gillian Leung, PharmD, BCCP; Yash Kothari, M.D 2023.

Prostacyclins: Adverse Events & Side Effects

Side Effects:

- Jaw pain
- Headache– acetaminophen
- Flushing/erythema
- Nausea– anti-emetic
- Diarrhea– loperamide
- Anorexia
- Thrombocytopenia



Complications of the Delivery System:

- Line sepsis
- EPO: Interruption (3–6 min)

Varies according to drug and route of delivery

Kingman, M, C. Archer-Chicko, M. Bartlett, J. Beckman et al. *Management of Prostacyclin Side Effects in Adult Patients with Pulmonary Arterial Hypertension.* Pulmonary Circulation DOI: 10.1177/2045893217715250 June 2017

Compliance Challenges

- Lower adherence with dosing frequencies of 3 or more times per day
- Diuretics: challenging to travelers or patients not homebound
- Repeated changes in dose and frequency can be confusing
- Rx that requires monthly lab testing (eg, bosentan, warfarin) may influence adherence due to inconvenience
- During long-term therapy, patients may develop physical/cognitive barriers
- Medication side effects

Stewart S. Pulmonary Hypertension Association. Available at: http://www.phaonlineuniv.org/Journal/Article.cfm?ItemNumber=786. Accessed: February 23, 2019.

Improving Compliance in PAH

- Assessment of medication adherence with every clinic visit
- Asking patients to bring pill bottles to reconcile meds initiated or discontinued between visits
- Utilization of pillboxes, timers, cell phone alarms, or notes for reminders
- Discussion of cultural concepts and social support
- Get the family involved: review perceived burden on family dynamics
- Consult with social services to address social or financial factors

Conclusions

- PAH is a disease resulting in restricted blood flow through the pulmonary arterial circulation resulting in increased pulmonary vascular resistance which causes an increased workload of the right ventricle and ultimately right heart failure
- Pathologic alterations in PAH include vascular proliferation, inflammation, fibrosis, and hypertrophy
- Scleroderma and methamphetamine are common causes of PAH
- Treatment of PAH now targets 4 known signaling pathways with the addition of 2 FDA therapies in 2024
- Disparities exist in the treatment of patients with PAH and consideration of patient perspectives should be central to the plan of care for patients
- Side effect management is imperative to improve patient compliance