

Optimizing Pulmonary Arterial Hypertension Management in Algeria: A Practical Adaptation of International Guidelines

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Abstract

Background: Pulmonary arterial hypertension (PAH) is a progressive disease with high morbidity and mortality. Although international guidelines recommend risk-based management, their implementation is often limited in resource-constrained settings.

Methods: We propose a pragmatic treatment algorithm based on **ESC/ERS 2025 guidelines** adapted to drug availability and healthcare organization in Algeria.

Results: The algorithm integrates initial dual therapy, escalation strategies, and emerging treatments such as sotatercept. A three-level care model is also proposed.

Conclusion: This approach may improve PAH management in low-resource settings.

INTRODUCTION

PAH is a rare but severe condition characterized by progressive pulmonary vascular remodeling leading to right heart failure [1,3,5]. Current **ESC/ERS guidelines**, including the most recent 2025 update, emphasize structured risk stratification and early combination therapy in PAH management, with tailored recommendations based on clinical risk and comorbidity profiles [1,2].

However, access to advanced therapies remains limited in many countries, including Algeria. This necessitates a pragmatic adaptation of international recommendations to real-world constraints, such as local drug availability and healthcare infrastructure [6,7].

Based on these guidelines, further treatment escalation is required if low-risk status is not achieved in scheduled follow-up assessments

MATERIALS AND METHODS

This work is based on international guidelines and recent studies, including the **ESC/ERS 2025 recommendations** [1–4,8,9], adapted to:

- Local drug availability
- Clinical practice constraints
- Healthcare infrastructure

We propose a risk-adapted treatment algorithm for newly diagnosed Group 1 PAH patients in Algeria. The objective is to improve functional and hemodynamic status and reduce disease progression.

PROPOSED ALGORITHM

1. Newly Diagnosed Patient (Group 1 PAH)

A. Low Risk

- Initial oral combination therapy: **Bosentan (ERA) + Sildenafil (PDE-5 inhibitor)** [1]
- Alternative: **Riociguat (Adempas):** Riociguat is a novel soluble guanylate cyclase (sGC) stimulator that is approved for the treatment of PAH and inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH). It is the first approved drug from the class of soluble guanylate cyclase (sGC) stimulators, which works by directly stimulating sGC and sensitizing it to endogenous nitric oxide to increase cyclic GMP production, resulting in vasodilation.

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- *Note: Riociguat should never be combined with Sildenafil due to risk of systemic hypotension [1,2].*

B. Intermediate Risk

- Initial oral combination therapy: Bosentan + Sildenafil or Bosentan + Riociguat [1]
- If insufficient response at 3–6 months, add:
 - **Sotatercept** (activin signaling inhibitor with antiproliferative effects) [3,4], Sotatercept is a first-in-class activin signaling inhibitor approved by the FDA and EMA in 2024 for the treatment of adults with pulmonary arterial hypertension (PAH), WHO Group 1.

- **Selexipag** (oral prostacyclin receptor agonist) [2,9]
- **Inhaled Iloprost** if Sotatercept is unavailable

C. High Risk

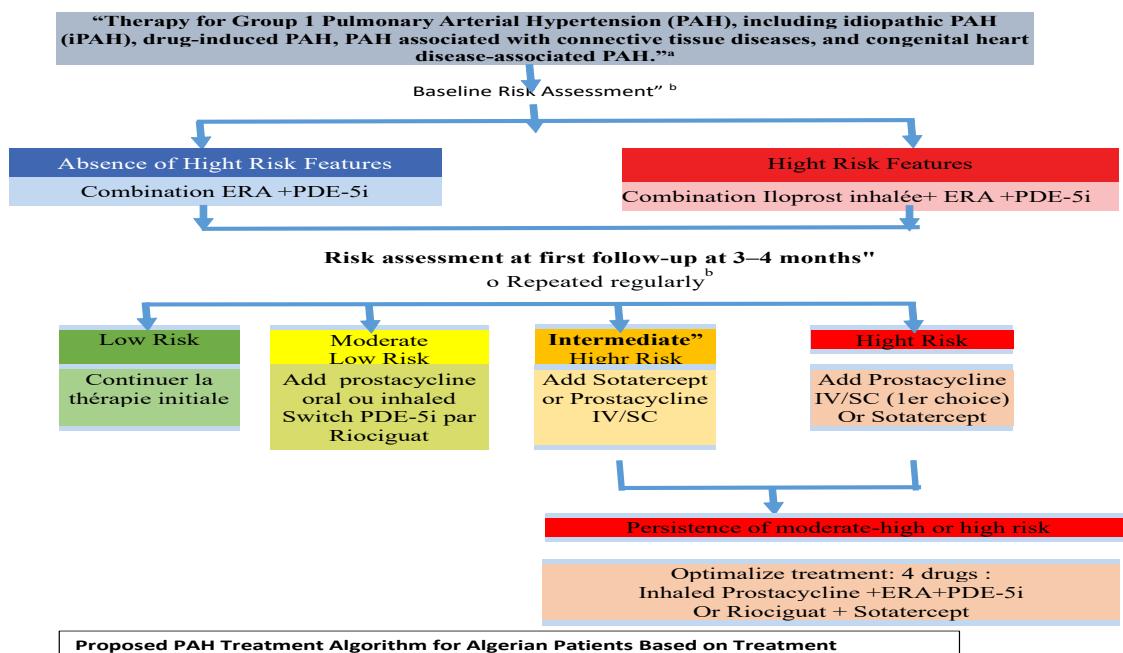
- Initial aggressive / rapid escalation strategy: **Triple therapy**
 - **Bosentan + Sildenafil (or Riociguat) + IV/SC prostacyclin** (oral not available in Algeria) [1]
- Sotatercept may be added as alternative or add-on in selected patients [3,4]
- Practical positioning per **ESC/ERS 2025**:
 - After insufficient dual oral therapy (intermediate risk) [1]

Table 1. PAH Treatment According to Initial Risk (Drugs Available in Algeria)

Risk Category	Drugs Available in Algeria
Low Risk	Bosentan, Riociguat, Sildenafil, Tadalafil
Intermediate Risk	Bosentan + Sildenafil/Tadalafil
High Risk	Iloprost inhaled ± Bosentan, Sildenafil, Tadalafil

Table 2. Detailed Risk-Based Recommendations

Risk Level	Recommended Treatment	Notes
Low Risk	Initial oral combination therapy: Bosentan + Sildenafil or Riociguat	Riociguat should never be combined with Sildenafil
Intermediate	Initial oral combination: Bosentan + Sildenafil or Bosentan + Riociguat; escalate: Sotatercept, Selexipag, Inhaled Iloprost	Improves hemodynamic status
High Risk	Triple therapy: Bosentan + Sildenafil (or Riociguat) + IV/SC prostacyclin; Sotatercept may be added	Quadruple therapy possible; alternative to parenteral prostacyclin



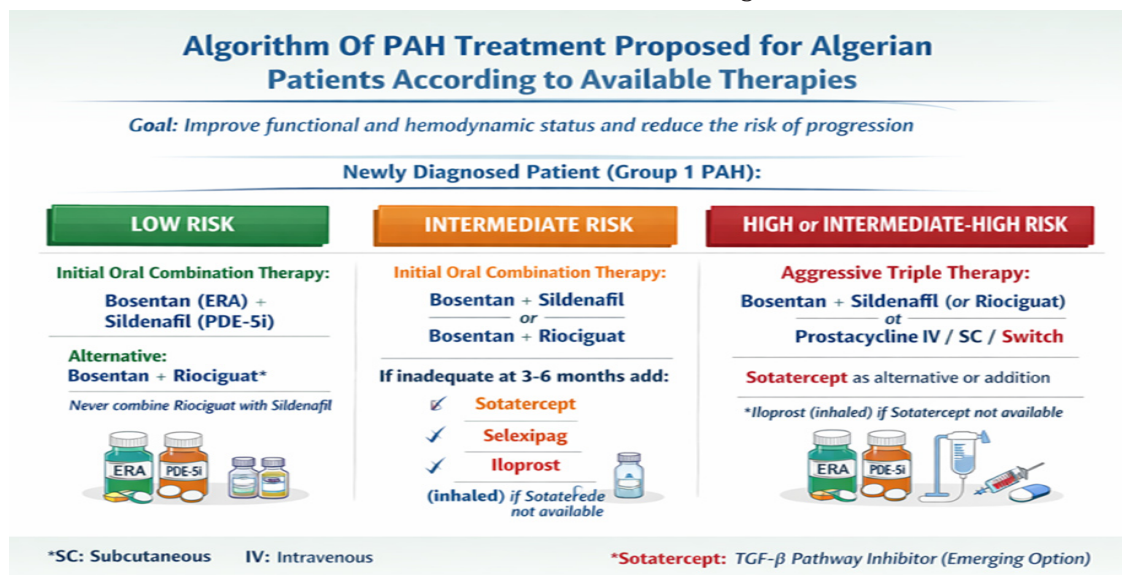
ERA: (Endothelin Receptor Antagonists), PDE-5i: (phosphodiesterase type 5 inhibitors)

- Alternative to parenteral prostacyclin depending on local availability [1]
- Quadruple therapy possible in expert centers according to national/regional practice

RESULTS (PROPOSED ALGORITHM)

Key Points:

- Initial dual therapy for low/intermediate risk patients improves outcomes compared to monotherapy [1,2,24].
- Early escalation when response is inadequate may prevent progression [1,2].
- Riociguat is a novel soluble guanylate cyclase (sGC) stimulator that is approved for the treatment of PAH and inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) and recently approved in Algeria. . It is the first approved drug from the class of soluble guanylate cyclase (sGC) stimulators, which works by directly stimulating sGC and sensitizing it to endogenous nitric oxide to increase cyclic GMP production, resulting in vasodilation.
- Integration of Sotatercept addresses residual risk and adds a novel mechanism targeting vascular remodelling [3,4].
- Sotatercept is a first-in-class activin signaling inhibitor approved by the FDA and EMA in 2024 for the treatment of adults with pulmonary arterial hypertension (PAH), WHO Group 1. It is administered as a subcutaneous injection every three weeks and is indicated to increase exercise capacity, improve WHO functional class, and reduce the risk of clinical worsening events when added to stable background



ERA: (Endothelin Receptor Antagonists), **PDE-5i:** (phosphodiesterase type 5 inhibitors)

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PAH therapy. The drug functions as a fusion protein (ActRIIA-Fc) that acts as a ligand trap for activins and growth differentiation factors (GDFs). By sequestering these pro-proliferative factors, sotatercept restores the balance between pro- and anti-proliferative signaling pathways in the pulmonary vasculature, thereby addressing the underlying vascular remodeling of PAH rather than merely causing vasodilation. Key clinical evidence includes the STELLAR phase 3 trial, which demonstrated significant improvements in six-minute walk distance, pulmonary vascular resistance, and WHO functional class in patients with WHO functional class II or III symptoms.

- Triple therapy remains standard for high-risk patients,

adapted to local availability and ESC/ERS 2025 risk stratification principles [1].

DISCUSSION

The proposed algorithm aligns with international recommendations while addressing real-world limitations. Combination therapy has significantly improved outcomes in PAH and is now recommended as first-line in most risk profiles [1,2,8]. However, access to prostacyclin analogues remains limited in Algeria; thus, alternatives such as **Selexipag** or **inhaled Iloprost** are important options.

Sotatercept represents a major advancement in PAH management due to its novel mechanism targeting vascular remodelling via the TGF-β/activin signalling

pathway [3,4]. Its inclusion in the algorithm provides an additional option in patients who do not achieve treatment goals despite dual or triple therapy.

The integration of **ESC/ERS 2025 recommendations** underscores the importance of dynamic risk stratification and therapy escalation, including personalized therapy selection based on response and tolerability [1].

CONCLUSIONS

This pragmatic algorithm provides a feasible strategy for PAH management in Algeria. Improving access to therapies and strengthening specialized centers remain key priorities.

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