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Pulmonary arterial hypertension:
A practical roadmap from diagnosis to treatment

Practice aid for PAH

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Clinical classification of PH[1]

Group 1: PAH

- **1.1** Idiopathic
- **1.2** Heritable
- **1.3** Associated with drugs and toxins
- **1.4** Associated with connective tissue disease, HIV infection, portal hypertension, congenital heart disease, schistosomiasis
- **1.5** PAH with features of venous/capillary (PVOD/PCH) involvement
- **1.6** Persistent PH of the newborn

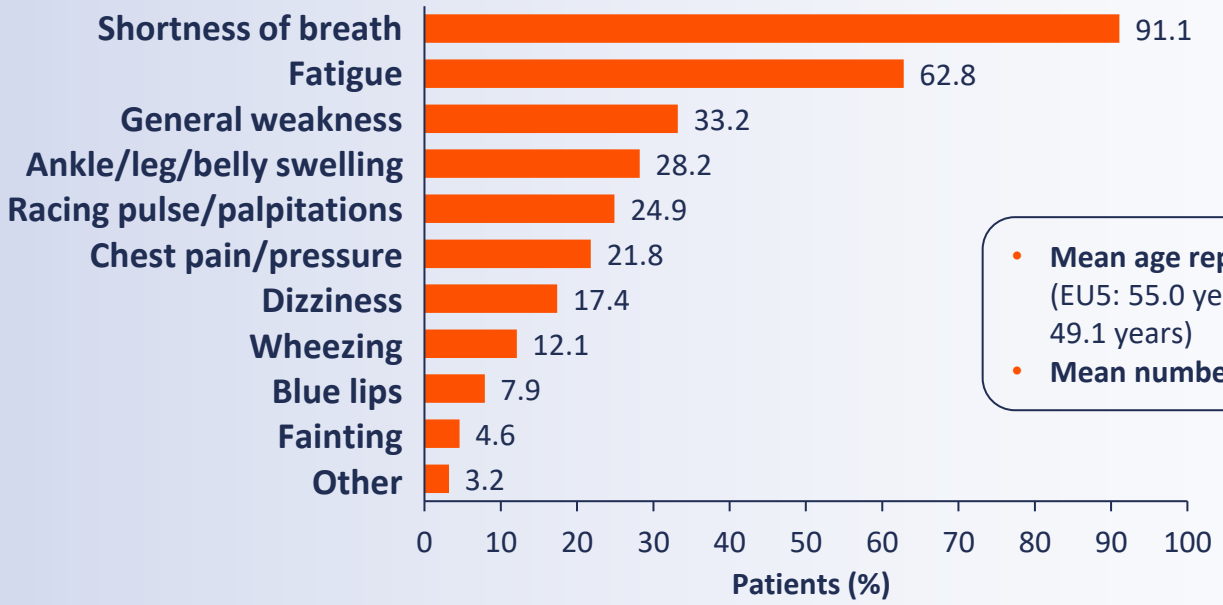
Group 2: PH associated with left heart disease

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

Group 4: PH associated with chronic pulmonary artery obstruction

Group 5: PH with unclear and/or multifactorial mechanisms

Symptoms of PAH first noticed by patients (N=572)[2]



- **Mean age reporting: 53.3 years** (EU5: 55.0 years; Japan: 54.2 years; USA: 49.1 years)
- **Mean number of symptoms: 3.1**

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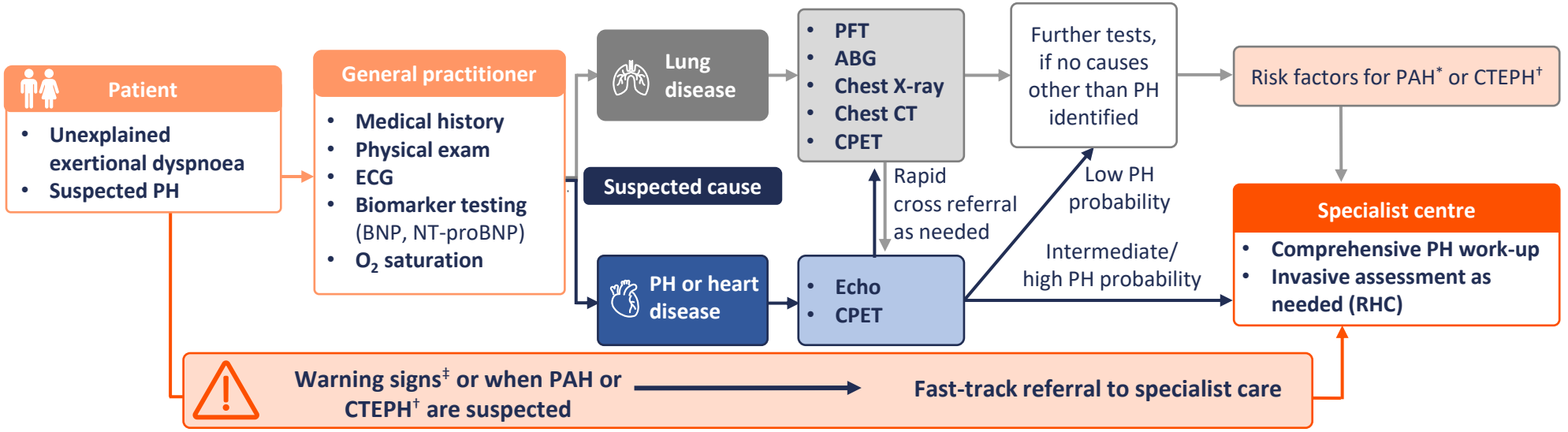
Diagnostic algorithm for PAH[1]



Treatment algorithm for PAH[1,3,4]

		Cardiopulmonary comorbidities	No cardiopulmonary comorbidities		
Initial	Risk§/ WHO-FCǁ	All	Low/intermediate	High	
	Therapy	Oral monotherapy: ERA or PDE5i	ERA + PDE5i	ERA + PDE5i + IV/SC PCA	
Follow-up	Risk§/ WHO-FCǁ	All	Low	Int.-low	Int.-high/high
	Therapy	Individualized therapy	Continue initial therapy	**Add** PRA or **Switch** PDE5i to sGC stimulator	**Add** IV/SC PCA and/or **Evaluate** for LTx

*Includes connective tissue disease (especially systemic sclerosis), portal hypertension, HIV infection, and family history of PAH. †A range of factors including a history of pulmonary embolism, IBD and essential thrombocythaemia. ‡Warning signs include rapid progression of symptoms, severely reduced exercise capacity, pre-syncope or syncope on mild exertion, signs of right heart failure. §ESC/ERS guidelines recommend using a 3-strata risk model pre-treatment and a 4-strata risk model when on treatment. ǁUS guidelines either emphasize WHO-FC class2 or REVEAL 2.03 to guide treatment selection.

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Agents for PAH: Newly approved or in phase III trials*

	Approved (USA and Europe, 2024[5,6])		In phase III clinical trials		
Agent	**Sotatercept**		**Ralinepag**	**MK-5475**	**Seralutinib**
MOA/Target	ACTRIIA ligand trap		PRA	sGC stimulator	TKI
Trial results/ Primary endpoint(s)	**Pivotal trial:** **NCT04576988 (STELLAR):** Change from BL in 6MWD vs placebo[7]	**Ongoing trials:** **NCT04896008 (ZENITH):** Time to first confirmed morbidity/mortality event[8] **NCT04796337 (SOTERIA):** Patients experiencing an AE[9] **NCT04811092 (HYPERION):** Time to clinical worsening[10]	**NCT03683186 (ADVANCE EXTENSION):** Patients with TEAEs[11] **NCT03626688 (ADVANCE OUTCOMES):** Time to first protocol-defined clinical worsening event[12]	**NCT04732221 (INSIGNIA-PAH):** Change from BL in 6MWD at 12 weeks[13]	**NCT05934526 (PROSERA):** Change from BL in 6MWD at 24 weeks[14] **NCT06274801 (PROSERA-EXT):** Incidence of TEAEs[15]
Completion date	Completed	**NCT04896008:** Nov 2025 **NCT04796337:** Nov 2027 **NCT04811092:** Dec 2029	**NCT03683186**: Sept 2024 **NCT03626688**: Dec 2024	Completed	**NCT05934526**: Oct 2025 **NCT06274801**: Dec 2026

*Information up-to-date as of October 2024.

Abbreviations and references

Abbreviations

6MWD, 6-minute walking distance; ABG, arterial blood gas analysis; ACTRIIA, activin receptor type IIA; AE, adverse event; BL, baseline; BNP, brain natriuretic peptide; CPET, cardiopulmonary exercise testing; CT, computed tomography; CTEPH, chronic thromboembolic PH; ECG, electrocardiogram; Echo, echocardiogram; ERA, endothelin receptor antagonist; ESC/ERS, European Society of Cardiology/European Respiratory Society; EU5, France, Germany, Italy, Spain, UK; IBD, inflammatory bowel disease; Int., intermediate; IV, intravenous; LTx, lung transplantation; MOA, mechanism of action; NT-proBNP, N-terminal pro-BNP; PAH, pulmonary arterial hypertension; PCA, prostacyclin analogue; PCH, pulmonary capillary haemangiomatosis; PDE5i, phosphodiesterase-5 inhibitor; PFT pulmonary function test; PH, pulmonary hypertension; PRA, prostacyclin receptor agonist; PVOD, pulmonary venoocclusive disease; RHC, right heart catheterization; REVEAL, Registry to Evaluate Early and Long-Term PAH Disease Management; SC, subcutaneous; sGC, soluble guanylate cyclase; TEAEs, treatment emergent AEs; TKI, tyrosine kinase inhibitor; WHO-FC, World Health Organization functional class.

References

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