

ELIGIBILITY CRITERIA FOR INITIATION OF PULMONARY ARTERIAL HYPERTENSION THERAPY

These guidelines are intended to assist relevant practitioners in gauging which patients are likely to be approved for pulmonary arterial hypertension treatments. In view of the complexity of pulmonary arterial hypertension diagnosis, classification and severity assessment, each application is thoroughly evaluated by the PAH Panel to determine the appropriateness of pulmonary vasodilator treatment.

Please note that the pharmaceuticals covered by these access criteria have different registered indications, and that some of the criteria included here are Unapproved Indications. If clinicians are intending to prescribe any of these pharmaceuticals for an Unapproved Indication, they should be aware of and comply with their obligations, including those set out in rule 4.6 of the Pharmaceutical Schedule.

All requested studies should be carried out in line with the relevant professional guidelines. Patients with pulmonary arterial hypertension who meet the following criteria may be eligible for initiation of pulmonary arterial hypertension treatment based on current clinical evidence.

The following treatments may be subsidised by application to the PAH Panel:

Category	Treatment
Endothelial receptor antagonists	Bosentan (Tracleer)
Phosphodiesterase type 5 inhibitors	Sildenafil (Viagra)
Prostacyclin analogues	Iloprost (Ventavis)

Patients eligible for initial approval of Special Authority

1. The patient must have a diagnosis of pulmonary arterial hypertension with the following WHO (Venice) clinical classifications:

- **Group 1**

- Idiopathic;
- Familial;
- Associated with:
 - Connective tissue disease;
 - Congenital systemic pulmonary shunts;
 - Portal hypertension;
 - HIV infection;
 - Drugs and toxins;
 - Other;
- Associated with significant venous or capillary involvement:
 - Pulmonary veno-occlusive disease (PVOD);
 - Pulmonary capillary haemangiomas (PCH);
- Persistent pulmonary hypertension of the newborn (PPHN)

- **Group 4**

- Pulmonary arterial hypertension due to thrombotic and/or embolic disease only)

- **Group 5**

- Miscellaneous group
E.g. sarcoidosis, histiocytosis X and lymphangiomatosis

Patients with PAH classified as group 2 or 3 are not eligible for subsidised treatment.

- **Group 2** - pulmonary hypertension associated with left heart disease

- **Group 3** - pulmonary hypertension associated with respiratory diseases and / or hypoxaemia

Lung function tests and cardiac function tests must be supplied with the initial application. For children under 10 years old, funding of sildenafil monotherapy will be considered using the data provided according to the application forms for children less than 10 years.

2. The patient must have NYHA/WHO functional class III or IV. For patients who are functional class II, applications will be considered in cases where there is clear evidence of disease progression (defined as a deterioration in performance of the 6MWT or deterioration in haemodynamic variables) despite current therapy.

Patients who are functional class I are not eligible for subsidised treatment.

New York Heart Association / World Health Organization Functional Classification of Pulmonary Hypertension	
Class I:	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnoea or fatigue, chest pain, or near syncope.
Class II:	Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity does not cause undue

	dyspnoea or fatigue, chest pain, or near syncope.
Class III:	Patients with pulmonary hypertension resulting in pronounced limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnoea or fatigue, chest pain, or near syncope.
Class IV:	Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnoea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

3. Right cardiac catheterisation data¹ must be supplied with the application. If cardiac catheterisation is contra-indicated, a letter of explanation is required. Unequivocal, significant evidence of raised pulmonary arterial pressure, in the absence of significant left heart disease, must be demonstrated.

- The patient must have a pulmonary capillary wedge pressure (PCWP) \leq 15 mmHg (patients with a PCWP between 15 mmHg and 18 mmHg may be considered at the Panel's discretion).
- The patient must have a mean pulmonary artery pressure (PAPm) $>$ 25 mmHg.
- An assessment of vasoreactivity has been carried out using iloprost, adenosine or nitric oxide. Where this assessment has not been carried out, applicants must provide reasons for this. (Vasoreactivity studies are not mandatory in patients with severe PAH (functional class IV or right atrial pressure $>$ 12 mmHg or Cardiac Index $<$ 2 l/min/m²) or PAH associated with connective tissue disease.)
- Where the patient has been shown to be vasoreactive (defined as a fall in mean PAP of greater than or equal to 10mmHg to less than 40mmHg with either an increase or no change in cardiac index), evidence of an adequate therapeutic trial of calcium channel blockers for three to six months must have been undertaken, followed by re-catheterisation demonstrating evidence of haemodynamic progression. (Due to the negative inotropic effects of CCBs, a trial of CCBs is not required in patients with severe disease as defined above.)

Treatment selection

Initial treatment:

- Patients who have not previously been treated with any of these agents would generally be expected to start treatment with sildenafil.
- NYHA WHO functional class IV patients who have been stabilised in hospital on iloprost would be able to receive iloprost in the community for a period of time to allow transition to sildenafil monotherapy, if clinically appropriate.

Change of treatment:

- Where sildenafil is not tolerated due to side-effects clinicians may apply for monotherapy with either bosentan or iloprost.

¹ Grossman, W (Ed). Cardiac Catheterization and Angiography, 3rd ed, Lea & Febiger, Philadelphia 1986

- Where the patient has not responded to sildenafil monotherapy, clinicians may apply for alternative monotherapy within 6 months of treatment initiation.

Patients eligible for renewal of Special Authority

Renewal applications must be submitted to the PAH Panel after six months of treatment approval, with annual reviews required thereafter.

Treatment selection

Renewal of treatment (stable patients):

- Patients who are stable or improve on PAH therapy will be considered for renewal of special authority.

Escalation of treatment:

- Eligibility for combination therapy for patients stable on treatment for at least six months who then deteriorate shall be determined by:
 - Clear evidence of deterioration in right heart cardiac catheterisation measures;
or
 - 15% deterioration in two 6MWTs done at least two weeks apart; or
 - NYHA/WHO functional class IV.
- Where patients show signs and symptoms of deterioration, and escalation of treatment is requested, a repeat right heart cardiac catheter is mandatory, except if the cardiac catheter is contraindicated, when a letter of explanation must be provided for the Panel to consider.
- Patients who have failed to respond to two monotherapies within the first six months of treatment may be eligible for combination therapy.
- Combination bosentan/iloprost may be considered for patients who cannot tolerate a sildenafil regime.
- Combination sildenafil/bosentan/iloprost therapy will not be approved.