ELIGIBILITY CRITERIA FOR PULMONARY ARTERIAL HYPERTENSION THERAPY

Contents

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These guidelines are intended to assist relevant practitioners in gauging which patients are likely to be approved for pulmonary arterial hypertension (PAH) treatments. Five treatments are currently funded for PAH. Of these, applications for two – sildenafil and bosentan – are through standard Special Authorities (SA), while the other three – ambrisentan, iloprost, and epoprostenol – are through Panel applications.

This document describes the general funded treatment pathway, including treatments both through regular Special Authorities and Panel applications. For sildenafil and bosentan, no application to the Panel is necessary. If a patient is seeking a treatment regimen that includes at least one of sildenafil and bosentan as well as a medicine covered by the Panel, please make a Panel application as well as completing a regular Special Authority form. Applications to the Panel may be made by a relevant specialist or a medical practitioner on the recommendation of a relevant specialist.

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 5.5 of the Pharmaceutical Schedule.

All requested tests 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.

MONOTHERAPY

A patient's first treatment must be monotherapy. A patient is expected to start on sildenafil monotherapy, unless they are:

a) A child with idiopathic PAH or PAH secondary to congenital heart disease, in which case they may start with bosentan monotherapy.
b) Intolerant of or contraindicated to sildenafil, in which case they may have bosentan monotherapy, or may apply to the Panel for ambrisentan, iloprost, or epoprostenol monotherapy. (Epoprostenol monotherapy may only be applied for in patients meeting the criteria described further below.)

A patient will need to complete three months of a monotherapy treatment before combination treatments will be considered.

DUAL THERAPY

To be eligible for dual therapy, a patient must either have:

- Tried a monotherapy for three months with no response, or
- Have deteriorated while on a monotherapy, as determined by:
    - Clear evidence of deterioration in right heart cardiac catheterisation measures; or
    - 15% deterioration in two 6 minute walk tests (6MWTs) done at least two weeks apart; or
    - NYHA/WHO functional class IV (the NYHA/WHO functional classification for PAH replicated on page 4).

For patients who are tolerant of sildenafil, one of the two agents must be sildenafil. Use of epoprostenol is restricted as described further below. Beyond that, clinicians may apply for any dual combination.

If a patient does not respond to a particular dual combination or deteriorates as described above, the clinician may apply for another dual therapy, noting the above restrictions still apply.

TRIPLE THERAPY

Triple therapy for patients on the lung transplant list

A patient on the lung transplant waiting list may apply for triple therapy. Any combination may be applied for, as long as sildenafil-tolerant patients include sildenafil as one of the three agents.

Triple therapy for patients for not on lung transplant list

A patient not on the lung transplant list may apply for triple therapy if:

a) The triple therapy would consist of sildenafil, bosentan, and any one other agent, and;
b) The patient meets any one of the following three criteria:

1. Patient presents acutely with idiopathic pulmonary arterial hypertension (IPAH) in New York Heart Association/World Health Organization (NYHA/WHO) Functional Class IV; or

2. Patient is deteriorating rapidly to NYHA/WHO Functional Class IV and may be a lung transplant recipient in the future, if their disease is stabilised; or

3. Patient has PAH associated with the scleroderma spectrum of diseases (APAHSSD) who have no major morbidities and are deteriorating despite combination therapy.

QUARDUPLE AND QUINTUPLE THERAPY

Treatments with four or more PAH agents are not funded.

USING EPOPROSTENOL WITHIN ONE OF THE ABOVE THERAPIES
Epoprostenol may only be applied for when patients meet one of the following criteria:

1. Patients presenting acutely with idiopathic pulmonary arterial hypertension (IPAH) in New York Heart Association/World Health Organization (NYHA/WHO) Functional Class IV; or
2. Patients deteriorating rapidly to NYHA/WHO Functional Class IV who may be lung transplant recipients in the future, if their disease is stabilised; or
3. Patients with PAH associated with the scleroderma spectrum of diseases (APAHSSD) who have no major morbidities and are deteriorating despite combination therapy, or
4. For use as a bridge to transplant for patients with pulmonary arterial hypertension who are on the active waiting list for lung transplantation.

Epoprostenol may be applied for as monotherapy or as part of a dual or triple therapy, provided all other conditions are met.

Patients eligible for approval of treatment by the PAH Panel

Where an application is put to the Panel for consideration (instead of through the standard Special Authorities), the following conditions must be met:

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 haemangiomatosis (PCH);
  - Persistent pulmonary hypertension of the newborn (PPHN) including:
    1. persistent pulmonary hypertension associated with premature/neonatal severe chronic lung disease or congenital diaphragmatic hernia
    2. infantile severe chronic lung disease where there is supportive evidence that the pulmonary vascular resistance had never normalised

- **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 first Panel application.

2. The patient must be in NYHA/WHO functional class II, III, or IV. 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 have 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 data [1] must be supplied with the application. If cardiac catheterisation is contraindicated, 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) ≤ 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 unless the patient is peri Fontan repair (see below).
    - The patient must have a pulmonary vascular resistance (PVR) of:
        - > 3 Wood Units; or
        - > 240 International Units (dyn s cm^{-5})
    - An assessment of vasoreactivity has been carried out using iloprost, adenosine or nitric oxide. Where this assessment has not been carried out, applicants must

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

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/m^2) 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.)

- For children peri Fontan repair, haemodynamic data is required and formal cardiac catheterisation should be considered at a clinically appropriate stage of the patient's management. Due to the presence of a non-pulsatile circuit a mean pulmonary artery pressure (PAPm) < 25mmHg would be acceptable.

4. Persistent pulmonary hypertension of the newborn associated with severe chronic lung disease (CLD) or congenital diaphragmatic hernia (CDH).

    - The application must include an inpatient management summary, admission history, echocardiogram, and short and long term management plan (including weaning plan).

    - Cardiac catheter should be considered for patients with CDH or CLD at a clinically appropriate stage of the patient's management where treatment is required for 12 months or more.

First Panel Application for Funding of Pulmonary Arterial Hypertension Treatments

- Use this form if this is the first time an application has been submitted to the PAH Panel for funding for this patient.
- Please complete as much of the form as possible, noting that not all questions will be relevant for children under 10 years old.

Please send applications to:

Email: PAH@pharmac.govt.nz

Post: PAH Panel Coordinator
PHARMAC
P O Box 10-254
WELLINGTON

Fax: 04 974 4858

Phone: 0800 023 588 option 5

Applications **must be complete** and accompanied by supporting data as required.

Have you attached:

- ☐ Cardiac catheterisation reports
- ☐ Lung function tests
- ☐ Echocardiography report
- ☐ Vasoreactivity data
- ☐ CCB trial results

Patient Details – patient sticker is acceptable			
Last name:			
First name/s:			
NHI number:			
Gender:	☐ Male ☐ Female ☐ Other		
Date of birth			
Address:			
Phone:	Home:	Work:	Mobile:
Email:			

Physician Details			
Full name:			
NZMC number:		Title	
Department or Practice address:			
Phone:			
Mobile:			
Fax:			
Email:			
Signature of applying physician:			

Requested regimen
☐ Monotherapy
☐ Dual therapy
☐ Triple therapy
Treatment(s) requested for Panel consideration
☐ Ambrisentan
☐ Iloprost
☐ Epoprostenol
Other PAH treatments that would be used with the above
☐ Sildenafil
☐ Bosentan

Prior treatments		
☐ This would be the patient's first treatment for PAH		
☐ The patient has previously trialled:		
Current or treatments tried	**Dose and duration**	**Response of the patient**

Please discuss the rationale for the proposed treatment regimen:

(if more space is required, please attach a separate document)

If sildenafil is not part of the proposed regimen, please explain why:

Basis of request for PAH treatments	
Diagnosis	**Tick**
Patient has been diagnosed as having pulmonary arterial hypertension	☐
NYHA/WHO functional class	
☐ 2 ☐ 3 ☐ 4	
WHO (Venice) clinical classification	
Group One – Pulmonary arterial hypertension	
Idiopathic PAH	☐
Familial PAH	☐
Associated with other diseases:	
Connective tissue disease	☐
Congenital systemic pulmonary shunts	☐
Portal hypertension	☐
HIV infection	☐
Drugs/toxins	☐
Other (specify):	☐
Associated with significant venous or capillary involvement	
Pulmonary veno-occlusive disease	☐
Pulmonary capillary haemangiomatosis	☐
Persistent pulmonary hypertension of the newborn	☐
Group Four – Pulmonary hypertension due to chronic thrombotic and/or embolic disease only	☐
Group Five – Other pulmonary hypertension (specify):	☐

Test results			
Height (cm):		Weight (kg):	
BMI (kg/m^2):		Blood pressure	

Lung function – Please report as actual values and percent predicted, and attach report

Date of test:

	Actual	Percent predicted
FEV_1		
FVC		
FEV_1/FVC (%)		
DLCO		
DLCO/VA		
TLC		

Six minute walk test:				Date of test:
Distance walked (m):				
SpO2:	Baseline:		Nadir:	
Heart Rate:	Baseline:		Maximum:	
Borg Index:	Pre:		Post:	
Brain natriuretic peptide (BNP):		BNP Reference Range:		

Information on patients under 10 years old			
Gestation at birth:		Birth weight (centile)	
Current oxygen use:			
Saturations	On room air	On oxygen at	Litres/min:
Results of overnight oximetry:			

Chest X-ray findings:		
	Actual	Percent predicted
FEV_1		
FVC		

Right Heart Cardiac Catheter (please attach reports)			
Date of test:		Testing centre:	
		Pre vasoreactivity testing	**Post vasoreactivity testing**
Pulmonary capillary wedge pressure: (Threshold ≤15 mmHg, or ≤18 mmHg at the Panel's discretion)			
Pulmonary artery pressures:	Mean:		
	Systolic:		
	Diastolic:		
Mean right atrial pressure:			
Pulmonary vascular resistance:	☐ Wood units (Threshold > 3)		
	☐ International units (Threshold >240)		
Cardiac output:			
Cardiac index:			

Vasoreactivity		
Has the patient been assessed for vasoreactivity using iloprost, adenosine or nitric oxide? If no, please provide reasons:	☐ Yes	☐ No

Cardiac catheterisation contraindicated:
Discussion:

Calcium channel blocker (CCB) history
• If the patient has idiopathic PAH, is vasoreactive, and has had a trial of CCBs for at least three months (preferably six), please attach re-catheterisation data demonstrating disease progression despite CCB treatment. • If necessary, please provide discussion of CCB treatment:

Echocardiography (please attach full report)	Date of test:
Echo RVP	
Echo RAP	

Medical History	
Transplant status:	☐ Not suitable for referral/turned down
	☐ Not yet referred
	☐ Inactive waiting list
	☐ Active waiting list
Smoking status:	☐ Smoker
	☐ Smoker and offered smoking cessation counselling and treatment
	☐ Ex-smoker — please state length of time:
	☐ Non-smoker

Current and relevant medications (including CCBs):

Comorbidities:

Would you like to make any other comments in support of this application?

Renewal Application or Request for Change of Therapy for Pulmonary Arterial Hypertension Treatments

- Use this form if this patient has previously been approved by the PAH Panel for funding.
- Please note that the criteria for funding of sildenafil and bosentan changed on 1 February 2018. An application to the PAH Panel is no longer necessary for those medications. Applications to the Panel are still required for all other PAH medications.

Please send applications to:

Email: PAH@pharmac.govt.nz

Post: PAH Panel Coordinator
PHARMAC
P O Box 10-254
WELLINGTON

Fax: 04 974 4858

Phone: 0800 023 588 option 5

Applications **must be complete** and accompanied by supporting data as required.

Have you attached:

- ☐ Cardiac catheterisation reports
- ☐ Lung function tests
- ☐ Echocardiography report
- ☐ Vasoreactivity data
- ☐ CCB trial results

Patient Details – patient sticker is acceptable			
Last name:			
First name/s:			
NHI number:			
Gender:	☐ Male ☐ Female ☐ Other		
Date of birth:			
Address:			
Phone:	Home:	Work:	Mobile:
Email:			

Physician Details			
Full name:			
NZMC number:		Title	
Department or Practice address:			
Phone:			
Mobile:			
Fax:			
Email:			
Signature of applying physician:		Date:	

Current treatments:	Dose:
☐ Sildenafil	
☐ Bosentan	
☐ Ambrisentan	
☐ Iloprost	
☐ Epoprostenol	

Change or continuation
☐ This is a request to continue a previously approved therapy: ☐ This is a request to change to a difference therapy, as below:
Requested regimen
☐ Monotherapy
☐ Dual therapy
☐ Triple therapy
Treatment(s) requested for Panel consideration
☐ Ambrisentan
☐ Iloprost
☐ Epoprostenol
Other PAH treatments that would be used with the above
☐ Sildenafil
☐ Bosentan

If applying for a change of therapy or combination therapy, please indicate reasons for change:

- ☐ Intolerance of current treatment (please provide details below)
- ☐ Lack of response to current treatment (please provide details below)
- ☐ Disease progression following previous disease stability (please provide details below)

Please discuss the rationale for requesting a change in treatment:

(if more space is required, please attach a separate document)

Status Update					
NYHA/WHO functional class					
☐ 2 ☐ 3 ☐ 4					
Test results					
Height (cm):		Weight (kg):			
BMI (kg/m^2):		Blood pressure			
Six minute walk test (x2 if annual renewal ie measured every six months):					
Distance walked (m):					
SpO2:	Baseline:		Nadir:		
Heart Rate:	Baseline:		Maximum:		
Borg Index:	Pre:		Post:		
Brain natriuretic peptide if available – please provide reference data:					
Right heart cardiac catheter (please attach report) All patients: Repeat cardiac catheter reports must be provided one year after the start of treatment. ▪ Stable patients: cardiac catheter reports are required at 2 to 4 year intervals depending upon patient progress. ▪ Unstable patients: Where escalation of treatment is requested, a repeat right heart cardiac catheter is mandatory.					
Testing centre:					
Pulmonary capillary wedge pressure: (Threshold ≤15 mmHg, or ≤18 mmHg at the Panel's discretion)					
Pulmonary artery pressures:	Mean:				
	Systolic:				
	Diastolic:				
Mean right atrial pressure:					
Pulmonary vascular resistance:	☐ Wood units (Threshold > 3)				
	☐ International units (Threshold >240)				
Cardiac output:					
Cardiac index					

Cardiac catheter contraindicated:	
Discussion:	
Echocardiography (please attach full report)	Date of test:
Echo RVP	
Echo RAP	

Current symptoms / general well-being over previous 6 or 12 months (as applicable)

(if more space is required, please attach a separate document)