



Australian Government

Medicare Australia

Physician's guide

Prescribing treatment for primary pulmonary hypertension and pulmonary arterial hypertension.

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Commonly used terms

Abbreviation or Term	
6MWT	six minute walk test
DoHA	Department of Health and Ageing
ECHO	echocardiography
HSDWP	Highly Specialised Drugs Working Party
IVC	inferior vena cava
mPVRI	mean pulmonary vascular resistance index
mPAP	mean pulmonary artery pressure
mRAP	mean right atrial pressure
PA systolic pressure	pulmonary arterial systolic pressure
PAH	pulmonary arterial hypertension
PAH agents	the group reference used in this document when referring to ambrisentan, bosentan monohydrate, iloprost trometamol, epoprostenol sodium and sildenafil citrate
PAH/SSc	pulmonary arterial hypertension associated with scleroderma
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PCWP	pulmonary capillary wedge pressure
PPH	primary pulmonary hypertension
RHC	right heart catheterisation
RV contractility	right ventricle contractility
RV size	right ventricle size
RVSP	right ventricular systolic pressure
TGA	Therapeutic Goods Administration
TR severity	tricuspid regurgitation severity
WHO	World Health Organization
WHO functional Class	World Health Organization functional Class

Introduction

This guide will provide you with information about prescribing Pharmaceutical Benefits Scheme (PBS) subsidised treatment for patients with ambrisentan, bosentan monohydrate, epoprostenol sodium, iloprost trometamol and sildenafil citrate (PAH agents).

This guide provides information on:

- eligibility requirements to prescribe these medicines as a PBS subsidy
- administrative requirements of Medicare Australia
- where to find more information and assistance from Medicare Australia
- restrictions for both initial and ongoing PBS subsidised treatment
- conditions and requirements for changing between the agents
- general guidelines on what constitutes stability and improvement in patient condition.

This version is current as of 1 April 2011 and will be updated as needed. Go to www.medicareaustralia.gov.au then **For health professionals > PBS > Specialised drugs (PBS) J-Z > Primary pulmonary and pulmonary arterial hypertension** to make sure you have the latest version.

Eligible prescribers and designated centres

In order to be eligible to prescribe a PAH agent as a PBS subsidised medicine, a prescriber must be from a designated centre. Designated centres are health facilities that have met criteria set by the Department of Health and Ageing (DoHA). Application process and selection criteria for designated centres are available by calling the Highly Specialised Drugs Working Party (HSDWP) Secretary on **02 6289 2331***.

Names of designated centres are available from www.medicareaustralia.gov.au then **For health professionals > PBS > Specialised drugs (PBS) J-Z > Primary pulmonary and pulmonary arterial hypertension** or by calling Medicare Australia on **1800 700 270**** (option 1).

Accessing forms and further information from Medicare Australia

Online

Copies of the application forms are available from www.medicareaustralia.gov.au then **For health professionals > PBS > Specialised drugs (PBS) J-Z > Primary pulmonary and pulmonary arterial hypertension**.

The complete PBS restrictions are available from www.pbs.gov.au

Assistance

If you need assistance or clarification call **1800 700 270**** (option 1) between 8.00am and 5.00pm EST, Monday to Friday.

Making an application to Medicare Australia

Applications for authority to prescribe these medicines as a PBS subsidised medicine must be made in writing using the relevant PAH authority application supporting information form available from www.medicareaustralia.gov.au then **For health professionals > PBS > Specialised drugs (PBS) J-Z > Primary pulmonary and pulmonary arterial hypertension**.

How to submit a written application

Written applications for authority to prescribe a PAH agent should be forwarded to:

Medicare Australia
Prior written approval of specialised drugs
Reply Paid 9826
Hobart TAS 7001

Hints and tips—prescribing PAH agents

- Delay in providing information to Medicare Australia Complex Drugs Unit will delay approval of PBS subsidised PAH agents.
- The forms used to apply must be the current version. Forms can be downloaded from www.medicareaustralia.gov.au then **For health professionals > PBS > Specialised drugs (PBS) J-Z > Primary pulmonary and pulmonary arterial hypertension** or call **1800 700 270**** (option 1).
- The original application documents are to be sent to Medicare Australia. Faxed or photocopied applications will not be approved.
- The requesting doctor must keep a complete copy of the application.
- Valid completed authority prescriptions must be sent to Medicare Australia along with the supporting information forms for each application. They must be completed by the doctor and contain the following:
 - authority prescription number on the top right hand side of the prescription
 - patient name
 - address
 - medicine name
 - dosage
 - quantity and repeats
 - doctor's signature
 - date.
- A valid prescription cannot be pre or post dated.
- Make sure the correct mailing address is written on the prescription as the approved authority prescription is to be returned to the patient or the prescriber.
- This program may be audited.
- There must, at all times, be continuity of testing procedures and Medicare Australia will be adhering to this requirement.

- To make sure there is continuity of treatment with a PAH agent, the timing of the continuing application to Medicare Australia should allow for waiting periods. This is to allow performance of the tests and receipt of the test results, receipt of the authorised prescription from Medicare Australia (around two weeks from mailing the application) and the dispensing process.
- The Medicare Australia team of pharmaceutical advisers will assess all applications. The time taken for assessment will depend on the quality of the information provided by the requesting doctor. Once all information is assessed and the eligibility of the patient for PBS subsidised benefits is determined, the prescription part of the application will be authorised and returned to either the patient or the doctor (doctor to indicate which option).
- Test comparisons are always against the patient's own baseline and not against the previous test.
- PAH agents are not PBS subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with scleroderma or connective tissue disease, where the total lung capacity is less than 70 per cent of that predicted.
- Under Section 100 arrangements, PAH agents are only available to a patient who is attending:
 - an approved private hospital
 - a public participating hospitalor
 - a public hospitaland is:
 - a day admitted patient
 - a non admitted patientor
 - a patient on discharge.
- PAH agents are not a PBS benefit for in-patients of the hospital.

Restrictions for PBS subsidised treatment

A patient must fully meet **one** of the following restriction criteria to attract PBS subsidy for a PAH agent. The application must be made by a prescriber from a designated centre.

The PAH agents and the relevant conditions are listed below.

Ambrisentan for the following conditions:

- I. I. World Health Organization (WHO) functional Class III or IV Primary Pulmonary Hypertension (PPH).
- II. II. WHO functional Class III or IV PAH secondary to connective tissue disease.

Bosentan monohydrate for the following conditions:

- I. WHO functional Class III or IV PPH.
- II. WHO functional Class III or IV PAH secondary to scleroderma.
- III. WHO functional Class III or IV PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology).

Epoprostenol sodium for the following conditions:

- I. WHO functional Class III PPH where the patient has failed to respond to an alternate PBS subsidised PAH agent.
- II. WHO functional Class IV PPH.

Iloprost trometamol for the following conditions:

- I. WHO functional Class III PPH or PAH secondary to connective tissue disease where the patient has failed to respond to an alternate PBS subsidised PAH agent.
- II. WHO functional Class IV PPH or PAH secondary to connective tissue disease.
- III. WHO functional Class III or IV drug induced PAH.

Sildenafil citrate for the following conditions:

- I. WHO functional Class III PPH.
- II. WHO functional Class III PAH secondary to connective tissue disease.

Note:

- Where the term 'PAH agent' appears, it refers to ambrisentan, bosentan monohydrate, epoprostenol sodium, iloprost trometamol and sildenafil citrate.
- Patients are eligible for PBS subsidised treatment with only one PAH agent at any time.
- Patients with pulmonary hypertension secondary to interstitial lung disease associated with scleroderma or connective tissue disease, where the total lung capacity is less than 70 per cent of that predicted, are not eligible for PBS subsidised treatment.
- Patients are not eligible to receive further PBS subsidised treatment with an agent to which they have previously failed to demonstrate stability or improvement.

- Patients with WHO functional Class III PPH may be eligible to interchange between ambrisentan, bosentan monohydrate, epoprostenol sodium (providing the patient has failed to respond to an alternate PBS subsidised PAH agent), iloprost trometamol, (providing the patient has failed to respond to an alternate PBS subsidised PAH agent) and sildenafil citrate.
- Patients with PPH with WHO Class IV severity may be eligible to interchange between ambrisentan, bosentan monohydrate, epoprostenol sodium and iloprost trometamol.
- Patients with WHO functional Class III PAH secondary to scleroderma may be eligible to interchange between ambrisentan, bosentan monohydrate, iloprost trometamol (providing the patient has failed to respond to an alternate PBS subsidised PAH agent) and sildenafil citrate.
- Patients with WHO functional class IV PAH secondary to scleroderma may be eligible to interchange between ambrisentan, bosentan monohydrate and iloprost trometamol.
- Patients with WHO functional Class III PAH secondary to connective tissue disease other than scleroderma may be eligible to interchange between ambrisentan, iloprost trometamol (providing the patient has failed to respond to an alternate PBS subsidised PAH agent) and sildenafil citrate.
- Patients with WHO functional Class IV PAH secondary to connective tissue disease other than scleroderma may be eligible for treatment with ambrisentan and iloprost trometamol.
- Patients with WHO Class III or IV drug induced PAH are eligible for treatment with iloprost trometamol only. They may not interchange between agents.
- Patients with PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology) are eligible for treatment with bosentan monohydrate only. They may not interchange between agents.

Prescribers should review the ambrisentan, bosentan monohydrate, epoprostenol sodium, iloprost trometamol and sildenafil citrate PBS Section 100 restriction criteria of the PBS Schedule available from www.pbs.gov.au

Medicine selection guide for primary pulmonary hypertension or pulmonary arterial hypertension

All patients must meet **one** of the following criteria.

1. WHO Class III with mean right atrial pressure (mRAP) **less than or equal to** 8 mmHg by right heart catheterisation (RHC) or as estimated by echocardiography (ECHO) and either:
 - inadequate response to appropriate vasodilator therapy
 - or**
 - intolerance / contraindication to vasodilators.
2. WHO Class III with mRAP **greater than** 8 mmHg via RHC or as estimated by ECHO
3. WHO Class IV.

Explanatory table regarding availability of PBS subsidised PAH medicine treatments

	Ambrisentan	Bosentan monohydrate	Iloprost trometamol	Epoprostenol sodium	Sildenafil citrate
PPH	✓	✓	✓ [‡]	✓ [‡]	✓ [†]
PAH 2 ^o to scleroderma	✓	✓	✓ [‡]	X	✓ [†]
PAH 2 ^o to connective tissue disease	✓	X	✓ [‡]	X	✓ [†]
PAH (drug induced)	X	X	✓	X	X
PAH associated with congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology)	X	✓	X	X	X

[†] WHO Class III only

[‡] WHO Class III patients must fail to respond to an alternate PBS subsidised PAH agent before being eligible to receive treatment with this agent

Interchangeability

Patients may swap between agents if:

- they meet the patient condition criteria noted above
- they have not previously failed to demonstrate stability or improvement to the agent to which they are swapping.

Authority approval requirements—initiation of PBS subsidised treatment—form 4138

Application forms for pulmonary arterial hypertension (PAH) agents are available from www.medicareaustralia.gov.au then **For health professionals > PBS > Specialised drugs (PBS) J-Z > Primary pulmonary and pulmonary arterial hypertension**

Applications must include signed patient and prescriber acknowledgements indicating the patient understands that PBS subsidised treatment with PAH agents will stop if the treating physician determines the patient has not demonstrated improvement or stability with treatment.

Applications for WHO functional Class III patients with mRAP less than or equal to 8 mmHg must include details of prior vasodilator treatment, including the dose and duration of treatment (minimum of six weeks). Where the patient experiences an adverse event or a contraindication to vasodilator treatment, the details according to the Therapeutic Goods Administration (TGA) approved Product Information must also be provided with the application.

Where fewer than three tests are able to be performed on clinical grounds, a patient specific reason outlining why the particular test/s could not be conducted must be provided with the authority application. Refer to '*Possible clinical grounds for the non-performance of RHC, ECHO or 6MWT*' in this guide.

Initiation of PBS subsidised treatment with bosentan monohydrate

All applications for initial treatment must be made in writing. You must include two separate authority prescriptions and submit to Medicare Australia for authorisation. The total of six months of PBS subsidised treatment will be approved with the first written application.

Approvals for the first authority prescription will be limited to one month of therapy with the 62.5 mg strength tablet, with the quantity approved based on the dosage recommendations in the TGA approved Product Information. No repeats will be authorised for this prescription. The second authority prescription can be written for either the 62.5 mg tablet or the 125 mg tablet strengths.

Medicare Australia will contact the prescriber two weeks after the date of the approval of the first authority prescription to confirm tablet strength before they send the second authority prescription to the prescriber. This will allow for the uninterrupted completion of the six month initial treatment course.

If the 62.5 mg tablet strength is needed, call **1800 700 270**** (option 1) for more information. Approvals for the second authority prescription will be limited to one month of treatment, with the quantity approved based on the dosage recommendations in the TGA approved Product Information and a maximum of four repeats.

Initiation of PBS subsidised treatment with all other PAH agents

Other PAH agents:

- ambrisentan
- epoprostenol sodium
- iloprost trometamol
- sildenafil citrate.

All applications for treatment must be made in writing.

The total duration of initial PBS subsidised treatment that will be approved with the first written application is up to six months, based on the dosage recommendation in the TGA approved Product Information.

For patients who are changing PAH agents (accessing interchangeability)

Application should be made using the *Continuation, change or demonstration of response to PBS subsidised treatment for PPH or PAH* form (form 4146), available from www.medicareaustralia.gov.au then **For health professionals > PBS > Specialised drugs (PBS) J-Z > Primary pulmonary and pulmonary arterial hypertension**

For more information, call **1800 700 270**** (option 1) between 8.00am and 5.00pm EST Monday to Friday.

Authority approval requirements

Continuation of treatment for all PAH agents—form 4146

Written applications for continuing treatment must be submitted to Medicare Australia for authorisation every six months. Approvals will be limited to provide sufficient supply for up to a maximum of six months of treatment, based on the dosage recommendations in the TGA approved Product Information.

Applications for continuing treatment will only be approved for patients who have demonstrated a response to the most recent course of treatment with the PAH agent for which an authority application is made.

The assessment of the patient's response to the first and subsequent six month courses of treatment should be made following the preceding five months of treatment, in order to allow sufficient time for a response to be demonstrated. Applications for continuing treatment with PAH agents should be made before the completion of the six month treatment course to make sure there is continuity for those patients who respond to treatment, as assessed by the treating physician.

Change between PAH agents—form 4146

For eligible patients, applications to change between PAH agents must be made under the relevant treatment restriction. All such applications must be accompanied by test results indicating the patient has responded to their most recent course of therapy with the medicine they are stopping. Where these results are not provided, patients will be deemed to have failed to demonstrate a response to therapy and may not receive further PBS subsidised treatment with that PAH agent.

Cessation of treatment

Patients who fail to demonstrate a response to a PBS subsidised PAH agent at the times where an assessment is needed must stop PBS subsidised therapy with that agent.

If patients are stopping treatment for reasons other than failure to demonstrate a response, prescribers are advised to submit a *Continuation, change or demonstration of response to PBS subsidised treatment for PPH or PAH* form (form 4146). If there is demonstration of adequate response or stability, this will enable patients to restart the relevant therapy at a later date if needed.

For patients stopping treatment of bosentan monohydrate, approval will be granted to provide sufficient supply of the 62.5 mg tablet strength to allow gradual dose reduction over a period of one month. Prescribers should call **1800 700 270**** (option 1) to receive authorisation for this final supply and to make sure no unintended break in treatment occurs.

Re-treatment with PAH agents

Patients who do not respond to treatment with a particular PAH agent are not eligible to receive further PBS subsidised treatment with that medicine under any circumstances.

Definition of conditions

Disease definitions

Primary pulmonary hypertension (PPH), drug-induced PAH, PAH secondary to connective tissue disease, including scleroderma and PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology) are defined as follows:

- (i) mean pulmonary artery pressure (mPAP) greater than 25 mmHg at rest and pulmonary capillary wedge pressure (PCWP) less than 18 mmHg
- (ii) mPAP greater than 30 mmHg with exercise and PCWP less than 18 mmHg

or

- (iii) where a RHC cannot be performed on clinical grounds, right ventricular systolic pressure (RVSP), assessed by ECHO, greater than 40 mmHg, with normal left ventricular function.

WHO functional Class III or IV disease severity

WHO functional Class III disease severity is:

patients with pulmonary hypertension resulting in marked limitation of physical activity who are comfortable at rest and on ordinary physical activity experience dyspnoea or fatigue, chest pain or near syncope.

WHO functional Class IV disease severity is:

patients with the 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.

Test requirements to establish baseline for initiation, response and continuation of treatment

Initiation of treatment

The first written application for PBS subsidised treatment with a PAH agent should be accompanied by the results of an RHC composite assessment, plus an ECHO composite assessment, plus a 6MWT to establish the patient's baseline measurements. These results will form the baseline against which response assessments will be made and must not be more than two months old at the time of application.

Where it is not possible to perform all three tests on clinical grounds, the following list outlines the preferred test combination, in descending order, for the purposes of initiation of PBS subsidised treatment:

1. RHC plus ECHO composite assessments
2. RHC composite assessment plus 6MWT
3. RHC composite assessment only.

In circumstances where a RHC cannot be performed on clinical grounds, applications may be sent to Medicare Australia for consideration based on the results of the following test combinations, which are listed in descending order of preference:

1. ECHO composite assessment plus 6MWT
2. ECHO composite assessment only.

Measurement of mRAP is preferentially performed by a RHC study. In those patients where RHC cannot be performed, an ECHO estimate is required to define those patients who should undergo a trial of vasodilator (defined as those patients with a mRAP less than or equal to 8 mmHg). ECHO criteria for an estimated mRAP of less than or equal to 8 mmHg are:

- inferior vena cava (IVC) diameter less than 2.5 cm
- change in IVC diameter of greater than 50 per cent with respiratory manoeuvres.

When less than three tests are able to be performed on clinical grounds, a patient specific reason outlining why the particular test/s could not be conducted must be provided with the authority application.

Where patients received treatment with ambrisentan, bosentan monohydrate, epoprostenol sodium, iloprost trometamol or sildenafil citrate before starting PBS subsidised treatment with the first of any of these PAH agents, the test requirements above still apply. The results that will form the baseline against which response assessments will be made will be those measured at the time patients started non PBS subsidised treatment with whichever PAH agent the patient received first.

Continuation of treatment

The following list outlines the preferred test combination, in descending order, for the purposes of continuation of PBS subsidised treatment:

1. RHC plus ECHO composite assessments plus 6MWT
2. RHC plus ECHO composite assessments
3. RHC composite assessment plus 6MWT
4. ECHO composite assessment plus 6MWT
5. RHC composite assessment only
6. ECHO composite assessment only.

Important

- The results of the same tests conducted at baseline should be provided with each written continuing treatment application (i.e. every six months), except for patients who were able to undergo all three tests at baseline, and whose subsequent ECHO and 6MWT results demonstrate disease stability or improvement, in which case RHC can be omitted.
- Test results provided are to be no more than two months old at the date of application. Therefore it is important to assess patients for their first continuation treatment after five months (but no earlier than four months). From that time, assessments should be made every six months.

Definition of response to a PAH agent or prior vasodilator treatment

For adult patients with two or more baseline tests, response to treatment is defined as two or more tests demonstrating stability or improvement of disease, as assessed by a physician from a designated centre.

For adult patients with a RHC composite assessment alone at baseline, response to treatment is defined as a RHC result demonstrating stability or improvement of disease, as assessed by a physician from a designated centre.

For adult patients with an ECHO composite assessment alone at baseline, response to treatment is defined as an ECHO result demonstrating stability or improvement of disease, as assessed by a physician from a designated centre.

For patients aged less than 18 years, response to treatment is defined as at least one of the baseline tests demonstrating stability or improvement of disease, as assessed by a physician from a designated centre.

Note: details of prior vasodilator treatment, including the dose and duration of treatment, must be provided at the time of application. If the patient has an adverse event or a contraindication to vasodilator treatment, details on the nature of the adverse event or contraindication according to the TGA approved Product Information must also be provided with the application.

Definition of stability or improvement using RHC, ECHO and 6MWT

Patients over 18 years of age

Definition of stability or improvement based on a RHC

Stability or improvement of the patient's condition using a RHC is defined as no more than 20 per cent deterioration from the baseline assessment on the overall composite of three or more of the following parameters:

- mRAP
- pulmonary arterial pressure
- pulmonary vascular resistance
- cardiac output +/- cardiac index
- pulmonary arterial oxygen saturation.

Definition of stability or improvement based on ECHO

Stability or improvement of the patient's condition using an ECHO is defined as no more than 20 per cent deterioration from the baseline assessment on the overall composite of three or more of the following parameters:

- tricuspid regurgitation severity
- pulmonary arterial acceleration time
- pulmonary arterial pressure—estimated right ventricular systolic pressure (RVSP)
- right ventricular size
- right ventricular contractility.

An experienced technician should perform the ECHO, and the report interpreted by a clinician with clinical experience in the field of pulmonary hypertension.

Definition of stability or improvement based on 6MWT

Stability or improvement of the patient's condition using a 6MWT is defined as no more than 20 per cent deterioration from the baseline assessment.

A suggested 6MWT protocol is provided for your reference in Appendix 7 of this guide.

Patients under 18 years

Definition of stability or improvement based on a RHC

Stability or improvement of the patient's condition based on an RHC is defined as at least one of the RHC parameters below showing no grade deterioration compared to baseline.

Note: no grade deterioration means there is no transition from one lesser severity category in the table below, to one of greater severity. For example, from normal to mild.

RHC parameters	Normal	Mild	Moderate	Severe
mRAP	< 8 mmHg	9-12 mmHg	13-18 mmHg	> 18 mmHg
mean cardiac index [#]	> 2.5 L/min/msq	2.0-2.5 L/min/msq	1.5-2.0 L/min/msq	< 1.5 L/min/msq
mean pulmonary vascular resistance index (PVRI) [#]	0-4U msq	4-8U msq	8-12U msq	> 12U msq

[#] Cardiac output and pulmonary vascular resistance must be indexed to body surface area.

Definition of stability or improvement based on ECHO

Stability or improvement of the patient's condition based on ECHO is defined as at least one of the parameters below showing no grade deterioration compared to baseline.

Note: no grade deterioration means there is no transition from one lesser grade category in the table below, to a higher graded category. For example, from Grade 1 to Grade 2.

ECHO parameters	Grade 1	Grade 2	Grade 3
right ventricle (RV) size	normal or mildly enlarged	moderately enlarged	markedly enlarged
RV contractility	normal or mildly depressed	moderately depressed	severely depressed
pulmonary arterial (PA) systolic pressure	below systemic	systemic [†]	greater than systemic
tricuspid regurgitation (TR) severity	absent or mild	moderate	severe

[†] Within 20 mmHg of systolic blood pressure.

Blood pressure must be taken at the same time to determine systemic pressure. These measures are based on expert clinical judgement.

Definition of stability or improvement based on a 6MWT

Stability or improvement of the patient's condition using a 6MWT is defined as a measurement of no more than 20 per cent deterioration from the baseline assessment.

A suggested 6MWT protocol is provided for your reference in Appendix 7 of this guide.

Possible clinical grounds for non-performance of RHC, ECHO or 6MWT

RHC

Note: this must be patient specific and provide full clinical details.

- Prohibitive access (clinically) to central venous blood vessels required for RHC.
- Clear safety reasons for avoidance of invasive procedure such as RHC. For example, infectious disease, direct risk of inducing critical instability, increased risk of procedure induced serious bleeding or thrombi (reiteration of these words is not sufficient, clinical details specific to the patient and reason must be supplied).

In children, RHC may also be omitted if patient has overt congestive heart failure or advanced right ventricular dysfunction.

ECHO

Note: this must be patient specific and provide full clinical details.

Prohibitive patient physique to clear reading of ECHO. For example, obesity, large breasts.

6MWT

Note: this must be patient specific and provide full clinical details.

The 6MWT is contraindicated in adults with moderate to severe mobility impairments that limit their ability to walk for six minutes consistently.

- Scleroderma may impact joint and limb movement.
- Amputation of one or more lower limbs.
- Other medical conditions that severely limit walking at required time of test. For example, unstable angina pectoris, psychiatric conditions and severe pain.
- Severe comprehension problems preventing accurate six minute walk testing.

In children, the 6MWT can also be excluded in patients aged less than 10 years and patients with congestive heart failure.

* Call charges apply.

** Call charges apply from mobile and pay phones only.

Appendix 1: Ambrisentan (Volibris®)

Ambrisentan (Volibris®) is manufactured by GlaxoSmithKline. It is an endothelin receptor antagonist and has been approved by the Pharmaceutical Benefits Scheme (PBS) for the treatment of primary pulmonary hypertension (PPH) and pulmonary arterial hypertension associated with connective tissue disease in patients with World Health Organization (WHO) Class III or IV severity.

Dosage and administration

Ambrisentan should be taken orally at a dose of 5 mg once daily. Additional benefit may result by increasing the dose to 10 mg.

There is no data available on the use of ambrisentan in patients under 18 years so its use in this age group is not recommended.

Note: ambrisentan is a category X medicine and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least three months following cessation of treatment with this medicine.

End of treatment

Patients who fail to demonstrate a response to PBS subsidised ambrisentan treatment at the times where an assessment is needed must stop PBS subsidised ambrisentan therapy.

For more information

For immediate medicine information or questions about ambrisentan contact:

GlaxoSmithKline Australia Pty Ltd
1061 Mountain Highway
Boronia VIC 3155
03 9721 6000*

www.gsk.com.au

For more information about restrictions call Medicare Australia **1800 700 270**** (option 1).

* Call charges apply.

** Call charges apply from mobile and pay phones only.

Appendix 2: Bosentan monohydrate (Tracleer®)

Bosentan monohydrate (Tracleer®) is manufactured by Actelion Pharmaceuticals, Australia. It is a dual endothelin-receptor antagonist agent, which is approved by the Therapeutic Goods Administration (TGA) and the Pharmaceutical Benefits Scheme (PBS) for the treatment of primary pulmonary hypertension (PPH), pulmonary arterial hypertension associated with scleroderma (PAH/SSc) or PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology) in patients with World Health Organization (WHO) Class III or IV severity.

Bosentan monohydrate therapy aims to improve symptoms and functional status, prevent disease progression and extend survival in patients with PPH and PAH/SSc.

TGA approved Product Information

The following dosage recommendations and other information are from the TGA approved Product Information for bosentan monohydrate. Refer to the current TGA approved bosentan monohydrate Product Information before prescribing.

	Starting dose (first four weeks)	Maintenance dose (week five onwards)
Adult > 40 kg Patients 18 years and under with a body weight > 40 kg	62.5 mg twice daily	125 mg twice daily
Adult < 40 kg (over 12 years) Patients 18 years and under with a body weight 20–40 kg	62.5 mg twice daily	62.5 mg twice daily
Patients 18 years and under with a body weight 10–20 kg	31.25 mg twice daily	62.5 mg twice daily
Patients 18 years and under with a body weight 10–20 kg	31.25 mg once daily	31.25 mg twice daily

Dosage adjustment in patients with low body weight

In patients with a body weight below 40 kg, but who are over 12 years of age, the recommended initial and maintenance dose is 62.5 mg twice daily.

Dosage adjustment in children

There is limited experience with the use of bosentan monohydrate in children. On the basis of the available information, the recommended doses in children aged three years and over are listed in the table above.

Doses above 125 mg twice daily do not appear to confer additional benefit sufficient to offset the increased risk of liver injury. Increased doses will not be PBS subsidised.

Note: bosentan monohydrate is a category X medicine and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least three months following cessation of treatment with this medicine.

Cessation of treatment

Patients who fail to demonstrate a response to PBS subsidised bosentan monohydrate treatment at the times where an assessment is needed must stop PBS subsidised bosentan monohydrate therapy.

For more information

The following website has been set up as a comprehensive resource for Australian clinicians and supporting health professionals and is updated regularly. Go to **www.actelionaustralia.com.au**

For immediate medicine information and questions about bosentan monohydrate contact:

Actelion Pharmaceuticals Australia

02 9486 4600* (during office hours)

0414 899 433* (after hours medical emergencies)

For more information about restrictions call Medicare Australia on **1800 700 270**** (option 1).

* Call charges apply.

** Call charges apply from mobile and pay phones only.

Appendix 3: Epoprostenol sodium (Flolan®)

Epoprostenol sodium (Flolan®) solution for injection, manufactured by GlaxoSmithKline Australia Pty Ltd, vasodilates pulmonary and systemic arterial vascular beds and inhibits platelet aggregation. It is listed on the Pharmaceutical Benefit Scheme (PBS) for the treatment of primary pulmonary hypertension (PPH) in patients with disease of World Health Organization (WHO) functional Class IV severity and for WHO functional Class III severity where the patient has failed to respond to an alternate PBS subsidised PAH agent. Epoprostenol sodium is administered by continuous intravenous infusion.

Epoprostenol sodium therapy aims to improve symptoms and functional status, prevent disease progression and extend survival in patients with PPH.

Dosage recommendations

Refer to current Therapeutic Goods Administration approved epoprostenol sodium Product Information before prescribing.

Cessation of treatment

Patients who fail to demonstrate a response to PBS subsidised epoprostenol sodium treatment, at the times where an assessment is needed, must stop PBS subsidised epoprostenol sodium therapy.

For more information

For immediate medicine information and questions about epoprostenol sodium contact:

GlaxoSmithKline Australia Pty Ltd
1061 Mountain Highway
Boronia VIC 3155
03 9721 6000*

For more information about restrictions call Medicare Australia on **1800 700 270**** (option 1).

* Call charges apply.

** Call charges apply from mobile and pay phones only.

Appendix 4: Iloprost trometamol (Ventavis®)

Iloprost trometamol (Ventavis®) for inhalation, manufactured by Schering Pty Ltd, is a synthetic prostacyclin analogue which is approved by the Pharmaceutical Benefit Scheme (PBS) for the treatment of primary pulmonary hypertension (PPH), drug induced pulmonary arterial hypertension (PAH) or PAH secondary to connective tissue disease with World Health Organization (WHO) functional Class IV severity, PPH, PAH secondary to connective tissue disease with WHO functional Class III severity where the patient has failed to respond to an alternate PBS subsidised PAH agent, and for drug induced PAH with WHO functional Class III severity.

Iloprost trometamol therapy aims to improve symptoms and functional status, prevent disease progression and extend survival in patients with PPH, drug induced PAH and PAH secondary to connective tissue disease.

Dosage recommendations

Refer to current Therapeutic Goods Administration approved iloprost trometamol Product Information before prescribing.

Adult dosage

Each inhalation session should start with 2.5 micrograms iloprost trometamol (as delivered at the mouthpiece of the inhalation device). The dose can be increased to 5.0 micrograms iloprost trometamol according to the individual need and tolerability.

The dose per inhalation session should be administered six to nine times per day according to individual need and tolerability.

Depending on the desired dose at the mouthpiece and on the nebuliser, the duration of an inhalation session is approximately five to 10 minutes.

Cessation of treatment

Patients who fail to demonstrate a response to PBS subsidised iloprost trometamol treatment at the times where an assessment is needed, must stop PBS subsidised iloprost trometamol therapy.

For more information

For immediate medicine information and questions about iloprost trometamol contact:

Schering Pty Ltd
02 9317 8666*

For more information about restrictions call Medicare Australia on **1800 700 270**** (option 1).

* Call charges apply.

** Call charges apply from mobile and pay phones only.

Appendix 5: Sildenafil citrate (Revatio®)

Sildenafil citrate (Revatio®) is manufactured by Pfizer Australia Pty Ltd. It is a selective inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type-5 and is approved by the Therapeutic Goods Administration (TGA) and the Pharmaceutical Benefit Scheme (PBS) for the treatment of patients with primary pulmonary hypertension (PPH) or pulmonary arterial hypertension (PAH) associated with connective tissue disease with World Health Organization (WHO) functional Class III severity.

Sildenafil citrate therapy aims to improve symptoms and functional status, prevent disease progression and extend survival in patients with WHO functional Class III disease.

Dosage recommendations

Refer to current TGA approved sildenafil citrate Product Information before prescribing.

Cessation of treatment

Patients who fail to demonstrate a response to PBS subsidised sildenafil citrate treatment at the times where an assessment is needed, must stop PBS subsidised sildenafil citrate therapy.

For more information

For immediate medicine information and questions about sildenafil citrate contact:

Pfizer Pty Limited
38-42 Wharf Road
West Ryde NSW 2144
02 9850 3333*

For more information about restrictions call Medicare Australia on **1800 700 270**** (option 1).

* Call charges apply.

** Call charges apply from mobile and pay phones only.

Appendix 6: Suggested six minute walk test protocol

The six minute walk test (6MWT) is a simple test performed to:

- assess a patient's level of fitness and how they are progressing with an exercise program
- assess a patient's fitness level in response to a medicine and/or a change in medicine (at the doctor's request)
- to see if a patient can start and/or continue on a certain medicine
- to assess the progression of a respiratory or cardiac disease (i.e. improvement or worsening of the patient's condition).

The measures or data are then used to determine a particular course that should be taken in the patient's treatment. For example, continue with a medicine, switch to another medicine or increase an exercise program.

A registered nurse or a physiotherapist usually conducts the test. It involves getting the patient to walk as many lengths of a 25 metre course as possible (sometimes 33 metres for clinical trials). The number of lengths the patient completes is counted to calculate the distance and the speed the patient walked during the test.

Before starting the test:

- the registered nurse/physiotherapist will need a 6MWT recording sheet, a stopwatch, a lap counter and a portable pulse oximeter
- the registered nurse/physiotherapist clearly explains to the patient what they need to do (i.e. complete as many lengths of the course as possible in six minutes). They are taken on a walk through the test itself
- a copy of the Borg Breathless scale also needs to be clearly displayed and explained to the patient. They are told to exercise at a level of between four and five on this scale. This means that they should be able to talk without undue difficulty during the test
- the patient's pulse and saturated oxygen levels are taken. The patient is told that they can stop and rest if they need to, and a chair is positioned near the course for this purpose
- discuss the warning signs, which include:
 - becoming short of breath
 - dizziness
 - chest pain
 - extreme fatigue
 - heart arrhythmia.

If the patient experiences any of these symptoms they should advise the registered nurse/physiotherapist and stop the test. The result will be recorded on the test sheet.