Agenda Item 9.01

POST-MARKET REVIEW (PMR) OF PULMONARY ARTERIAL HYPERTENSION (PAH) MEDICINES: REVISED PBS RESTRICTIONS AND ESTIMATED COSTS TO THE PBS

1 Purpose of Application

The PBAC was requested to:

1.1 **Consider and accept** the revised PBS restrictions for currently listed endothelin receptor antagonist (ERAs) and phosphodiesterase-5 (PDE-5) inhibitor medicines to extend subsidised monotherapy to patients with WHO Functional Class (FC) II pulmonary arterial hypertension (PAH).

1.2 **Consider and accept** the additional restriction changes to all PBS listed PAH medicines relating to: PAH terminology; the inclusion of additional PAH sub-types; removal of the requirement to trial calcium channel blockers; and strengthening the diagnostic role of right heart catherisation (RHC).

1.3 **Consider and comment** on the estimated cost to the PBS as a consequence of extending subsidised treatment with ERAs (bosentan, ambrisentan, macitentan) and PDE-5 inhibitors (sildenafil, tadalafil) to patients presenting with WHO FC II PAH.

2 Background

2.1 At the November 2018 meeting, the PBAC considered the Post-market Review (PMR) of PAH Medicines report and the six Review Options developed by the PAH Reference Group during the Review. The following is a brief summary of the PBAC recommendations for each of the Review Options:

- Extend the subsidy of PBS listed ERAs (bosentan, ambrisentan and macitentan) and PDE-5 inhibitors (sildenafil and tadalafil), to patients in WHO FC II as monotherapy. The PBAC requested that revised restrictions and estimated costs of extending treatment to patients with WHO FC II symptoms be brought back to the PBAC prior to making a final recommendation (Option 1).
- PBS subsidised dual combination PAH therapy was not recommended for patients presenting with WHO FC II symptoms (Option 2).
- That a stakeholder meeting would be required to progress any recommendation for combination therapy with ERAs and PDE-5 inhibitors for patients with WHO FC III/IV symptoms (Option 3).
- Align the PBS restrictions with clinical guidelines by removing the current requirement to trial a vasodilator (calcium channel blocker) and strengthen the requirement to perform RHC for the diagnosis of PAH

(Option 4).

- Amend the PBS restrictions for all PAH targeted medicines to include all WHO Group 1 PAH subtypes (Option 5).
- Review the guidelines/criteria for establishing a PAH designated prescribing centre, particularly with regard to annual numbers of patients and available clinical expertise (Option 6).

3 Current Situation

Revised PBS restrictions - Options 1, 4 & 5

3.1 As requested at the November 2018 meeting, the PBAC recommended changes to extend the PBS restrictions for monotherapy with ERAs and PDE-5 inhibitors to patients in WHO FC II were drafted. The draft restrictions were circulated to the Reference Group and medicine sponsors prior to presentation to the PBAC at the March 2019 PBAC meeting.

3.2 The PBS restrictions for all PAH targeted medicines were amended as recommended at the November 2018 PBAC meeting , by:

- removing the need for failed vasodilator treatment (Option 4)
- introducing the requirement for a second opinion where the treating clinician considers that RHC cannot be performed on clinical grounds (Option 4)
- including the remaining WHO Group I PAH subtypes (Option 5) and
- updating the definition of PAH in line with international guidelines.

3.3 During the pre-March PBAC 2019 consultation process, the Reference Group suggested the PBS restriction definition for all PAH medicines be updated to align with the 2015 European Society of Cardiology /European Respiratory Society (ESC/ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension. The Reference Group requested that the definition of PAH be amended to **(*changes in italics*):**

'mean pulmonary arterial pressure (mPAP) greater than *or equal to* 25 mmHg at rest and pulmonary artery wedge pressure (PAWP) less than *or equal to* 15 mmHg'.

3.3 Reference to designated PAH centres in the PBS restrictions was aligned with the terminology used for the centres on the Department of Human Services website.

3.4 The PBAC was advised that the PBS restrictions for ERAs, PDE-5 inhibitors, iloprost and riociguat currently include six separate restrictions for specific treatment phases. The PBS restrictions for bosentan include an additional restriction for cessation of treatment. Application of the November 2018 recommended amendments to the PBS PAH restrictions resulted in the current Initial 2 (new patients) restriction becoming redundant (Initial 1 for iloprost) for all PAH medicines as shown in Table 1. Epoprostenol is the exception, retaining its current five restrictions.

Table 1: Overview of Revised PBS restrictions

Current Restrictions - Treatment Phases	Draft Revised Restrictions Treatment Phases
Initial 1 (new patients)	Initial 1 (new patients)
Initial 2 (new patients)	~~Initial 2 (new patients)~~
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)
First Continuing treatment	First Continuing treatment
Subsequent Continuing treatment	Subsequent Continuing treatment
Cessation of treatment (all patients) (bosentan only)	Cessation of treatment (all patients) (bosentan only)
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply

Combination therapy and Stakeholder Meeting - Option 3

3.5 The Department advised that a sponsor and stakeholder meeting to progress appropriate PBS restrictions and subsidy conditions for PAH combination therapy is planned for May 2019.

Guidelines for establishing designated PAH centres - Option 6

3.6 The Department advised a review of the PAH Designated Prescribing Centre guidelines in consultation with the Medical Adviser, Technology Assessment and Access Division had commenced. It was anticipated that the review findings would be available for consideration at the July 2019 PBAC meeting.

Pre-PBAC responses

3.7 All sponsors of PBS subsidised PAH targeted medicines were provided with the revised PBS restrictions and given the opportunity to provide a pre-PBAC response. Responses were received from Actelion and GlaxoSmithKline (GSK). Pfizer acknowledged the opportunity to provide a response.

3.8 Both sponsors were supportive of the changes to the restrictions and of the potential to make PBS subsidised combination therapy with ERAs and PDE-5 inhibitor medicines available to the identified PAH patient populations. One sponsor, GSK, proposed further changes to the PBS restrictions for epoprostenol to better align subsidised use of this medicine with clinical guidelines. GSK suggested that the Initial 1 (new patient) PBS restriction for epoprostenol be amended to include 'treatment of patients with WHO Functional Class III PAH with evidence of rapid progression of their disease or other markers or poor prognosis'.

3.9 The sponsor stated this is consistent with the 2015 European Society of Cardiology and European Respiratory Society Guidelines for the diagnosis and treatment of pulmonary hypertension and the American College of Chest Physicians Guideline and Expert Panel Report on Pharmacotherapy.

4 Estimated cost to the PBS of extending PBS subsidy to patients with WHO FC II symptoms

4.1 Estimates were prepared by the Post-market Review Section in consultation with the Drug Utilisation Sub-Committee Secretariat.

4.2 The PBAC was advised that the estimated cost impact of extending PBS subsidised monotherapy with ERAs and PDE-5 inhibitors to patients presenting with WHO FC II PAH symptoms was expected to range from approximately $2.7 million in 2019 to $3.5 million in 2023.

4.3 The estimated annual cost to the PBS took a market share approach based on the incident population currently receiving PBS PAH medicines in 2018.

The following assumptions underpinned the model:

Incident patient numbers

4.4 The additional incident population presenting for treatment in WHO FC II would be approximately 20% of the incident population in WHO FC III-IV, which ranged from 440 in 2014 to 504 in 2018 based on PBS data.

4.5 It was assumed that 90% of incident patients diagnosed in WHO FC II will take up treatment.

4.6 The projected number of incident and treated patients in WHO FC II is presented in Table 2 below and ranges from 112 patients in 2019 to 119 patients in 2023.

Table 2: Estimated incident population in WHO FC II

Year	2019	2020	2021	2022	2023
Estimated number of incident treated patients in WHO FC III-IV	503	511	520	528	537
Estimated number of incident patients in WHO FC II	124	126	128	131	133
Treated incident patients in WHO FC II	112	114	116	118	119

Prevalent patient numbers

4.7 It was assumed that a prevalent pool of patients with WHO FC II PAH symptoms exists and that 50% would already be treated with PBS subsidised PAH medicines.

4.8 The prevalent population was modelled over four years by assuming 50% of incident patients would deteriorate to WHO FC III-IV each year and 50% would remain in the prevalent FC ll group.

Treated patient population

4.9 The total number of treated patients in WHO FC II was estimated to be 173 in 2019, increasing to 244 in 2023 as shown in Table 3.

Table 3: Treated population in WHO FC II

Year	2019	2020	2021	2022	2023
Number of incident patients	112	114	116	118	119
Number of prevalent patients *	61	93	109	118	124
Total number of patients	173	206	225	235	244

** Prevalent population assumes 50% remain in WHO FC II into the subsequent year and 50% move into the currently funded WHO FC III/IV population.*

PBS/RPBS Cost of PAH Medicines

4.10 Forecast PBS costs were obtained from the pricing area of the Department for all PBS listed ERAs and PDE-5 inhibitors from 2019 to July 2023. Several of these medicines are off patent (F2) and subject to ongoing price disclosure price reductions. Table 4 shows the average cost to the PBS/RPBS per prescription for each of the medicines.

[redacted]

Scenarios – total financial impact to PBS

4.11 Two scenarios based on different initiation rates of ERAs and PDE-5 inhibitors across the newly treated WHO FC II population were provided. In the base case, the uptake rate for each ERA and PDE-5 inhibitor reflects the current rate PBS PAH medicines are used as initial therapy in WHO FC III/IV (2018). Scenario 2 doubles the proportion of PDE-5 inhibitors and reduces the incident uptake of ERAs accordingly. Table 5 provides the modelled uptake rates of PAH medicines in patients with WHO FC II symptoms.

[redacted]

4.12 Estimated prescription numbers per year were applied separately to incident and prevalent patients.

- The number of prescriptions dispensed to prevalent patients in WHO FC II was estimated to be 9.95/year based on the average number of PAH medicine dispensings/patient in the WHO FC III/IV PBS treated population between 2016 and 2018.
- The number of prescriptions dispensed to incident patients was estimated to be an average of 5/year as patients are expected to commence treatment at any time throughout a year.

Estimated Cost to the PBS/RPBS for subsidising ERAs and PDE-5 inhibitors for patients presenting in WHO FC II (Option 2)

4.13 The PBAC was advised that the additional cost to the PBS/RPBS was estimated to be approximately $13 million for the Base Case and approximately $10 million for Scenario 2, over the first four years of listing.

Table 6: Estimated cost for monotherapy in WHO FC II

Year	2019	2020	2021	2022	2023	Total (2019 – 2022)
Net cost to PBS/RPBS Base Case	**$2,692,486**	**$3,238,184**	**$3,409,348**	**$3,442,534**	**$3,508,900**	**$12,782,552**
Scenario 2	$2,089,691	$2,520,159	$2,662,511	$2,695,231	$2,748,257	$9,967,592

5 PBAC Outcome

5.1 The PBAC considered and accepted that the estimated cost of of extending PBS subsidised monotherapy with ERAs and PDE-5 inhibitors to patients presenting with WHO FC II PAH symptoms ranges from approximately approximately $2.7 million in 2019 to $3.5 million in 2023. The PBAC considered the underlying assumptions used in the modelling for the cost estimates were reasonable. The PBAC noted the estimated annual cost to the PBS was acceptable given the high clinical need and the evidence that ERAs and PDE-5 inhibitors are effective in patients presenting with WHO FC ll symptoms and may delay patients deteriorating to WHO FC lll/lV. The PBAC reviewed and accepted the revised PBS restrictions to extend subsidy to patients in WHO FC II PAH for monotherapy with ERAs and PDE-5 inhibitors medicines as recommended at the November 2018 meeting.

5.2 The PBAC also reviewed and accepted the November 2018 recommended additional restriction changes to all PBS listed PAH medicines relating to: PAH terminology; the inclusion of additional PAH sub-types; removal of the requirement to trial calcium channel blockers; and strengthening the diagnostic role of right heart catherisation (RHC).

5.3 The PBAC accepted the amendment to the PBS restriction definition for PAH as proposed by the Reference Group to better align PBS restrictions with clinical guidelines. The definition for PAH in the PBS restrictions should be amended to:

'mean pulmonary arterial pressure (mPAP) greater than or equal to 25 mmHg at rest and pulmonary artery wedge pressure (PAWP) less than or equal to 15 mmHg'.

5.4 The PBAC noted the pre-PBAC responses from sponsors, and in particular the request from GSK to extend subsidy of epoprostenol to "initial treatment in patients with WHO FC III symptoms who have evidence of rapid progression of their disease or other markers of a poor prognosis". The PBAC noted that epoprostenol is currently PBS subsidised as second line treatment for patients with WHO FC III symptoms and first line for patients with WHO FC IV symptoms.

5.5 The PBAC was of a mind to extend the subsdidy of epoprostenol to include first line treatment for patients with WHO FC III PAH at high risk of deterioration. The PBAC requested further information on this proposal, including on criteria to determine 'evidence of rapid progression of their disease or other markers of a poor prognosis'. The flow-on effect to iloprost, the other PBS listed prostanoid, of any proposal to extend the subsidy of epoprostenol to first line treatment for these patients would need to be considered.

5.6 The PBAC noted that the Department intends to progress a stakeholder meeting to discuss potential dual combination (initial and/or sequential combination) PBS subsidised therapy with ERAs and PDE-5 inhibitor medicines for patients with WHO FC III/IV PAH symptoms with increased risk factors or evidence of rapid deterioration in their condition. The PBAC recalled that progression of PBS subsidy for dual combination therapy would be dependant on achievement of an acceptable price and that sponsors had previously supported a stakeholder meeting to address this. This stakeholder meeting may also be used to progress the request in 5.4 above to extend the PBS listing for epoprostenol in patients with WHO FC lll symptoms.

5.7 The PBAC noted Department advice that a review of the PAH Designated Prescribing Centre guidelines had commenced. Review findings should be available for consideration at the July 2019 PBAC meeting.

6 Recommended Listing

The recommended amended restrictions for all eight PAH targeted medicines (bosentan, ambrisentan, macitentan, sildenafil, tadalafil, epoprostenol, iloprost and riociguat) are complex. For conciseness, where revised restrictions are common to multiple listings, they are presented once only and referenced where appropriate.

6.1 BOSENTAN

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
BOSENTAN						
62.5MG TABLET S100 HSD Public	5618Q	1	0	$1536.56	All brands	All manufacturers
62.5MG TABLET S100 HSD Private	6429J	1	0	$1583.85		
125MG TABLET S100 HSD Public	5619R	1	0	$1536.56		
125MG TABLET S100 HSD Private	6430K	1	0	$1583.85		

The revised PBS restrictions for bosentan have six treatment phases instead of the previous seven treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions - Treatment Phases	Revised Restrictions Treatment Phases	Restriction Location within this Document
Initial 1 (new patients)	Initial 1 (new patients)	6.1.1
Initial 2 (new patients)	~~Initial 2 (new patients)~~	6.1.2 (deleted)
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.1.3
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Cessation of treatment (all patients) (bosentan only)	Cessation of treatment (all patients) (bosentan only)	6.1.4
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Refer 6.9.3

Amend existing/recommended listing of bosentan as follows:

Changes appear in *italics* and ~~strikethrough~~

6.1.1 Treatment Phase: Initial 1 (new patients)-bosentan

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Treatment Phase: Initial 1 (new patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent, **AND** Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** *Patient must have WHO Functional Class II PAH, or WHO Functional Class III PAH, or WHO Functional Class IV PAH,* ~~Patient must have WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class III pulmonary arterial hypertension secondary to connective tissue disease,~~ ~~**AND**~~ ~~Patient must have a mean right atrial pressure of 8 mmHg or less as measured by right heart catheterisation (RHC); OR~~ ~~Patient must have right ventricular function assessed by echocardiography (ECHO) where a RHC cannot be performed on clinical grounds,~~ ~~**AND**~~ ~~Patient must have failed to respond to 6 or more weeks of appropriate vasodilator treatment unless intolerance or a contraindication to such treatment exists,~~ **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*

	○ *Congenital heart disease* ○ *Schistosomiasis*
Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) two completed authority prescription forms; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form which includes results from the three tests below, where available: (i) RHC composite assessment; and (ii) ECHO composite assessment; and (iii) 6 Minute Walk Test (6MWT); and (3) a signed patient acknowledgement. ~~Idiopathic pulmonary arterial hypertension, anorexigen-induced pulmonary arterial hypertension, hereditable pulmonary arterial hypertension, drug-induced pulmonary arterial hypertension, pulmonary arterial hypertension secondary to connective tissue disease including scleroderma, or pulmonary arterial hypertension associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology) are defined as follows:~~ *PAH (WHO Group I pulmonary hypertension) is defined as follows:* (i) mean pulmonary artery pressure (mPAP) greater than *or equal to* 25 mmHg at rest and pulmonary artery wedge pressure (PAWP) less than *or equal to* 15 mmHg; or (ii) where a right heart catheter (RHC) cannot be performed on clinical grounds, right ventricular systolic pressure (RVSP), assessed by echocardiography (ECHO), greater than 40 mmHg, with normal left ventricular function. ~~Test requirements to establish baseline for initiation of treatment are as follows:~~ The first written application for PBS-subsidised treatment with the first PAH agent should be accompanied by the results of a right heart catheter (RHC) composite assessment plus an echocardiograph (ECHO) composite assessment, plus a 6 minute walk test (6MWT) to establish the patient's baseline measurements. Where it is not possible to perform all 3 tests above 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 submitted 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. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. ~~Details of prior vasodilator treatment, including the dose and duration of treatment, must be provided at the time of application. Where the patient has an adverse event to a vasodilator or where vasodilator treatment is contraindicated, details of the nature of the adverse event or contraindication according to the Therapeutic Goods Administration (TGA) approved Product Information must also be provided with the application.~~

	~~Response to prior vasodilator treatment is defined as follows:~~ ~~For patients with 2 or more baseline tests, response to treatment is defined as 2 or more tests demonstrating stability or improvement of disease, as assessed by a physician from a designated hospital.~~ ~~For 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 hospital.~~ ~~For 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 hospital.~~ ~~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 hospital.~~ Approvals for the first authority prescription will be limited to 1 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 may be written for either the 62.5 mg tablet or the 125 mg tablet strengths. Approvals for the second authority prescription will be limited to 1 month of treatment, with the quantity approved based on the dosage recommendations in the TGA-approved Product Information, and a maximum of 4 repeats. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted.
Administrative Advice	**Note** Where the 62.5 mg tablet strength is required for the second authority prescription, please contact the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday) for further advice. The approved second authority prescription will be returned to the prescriber by the Department of Human Services two weeks after the date of the approval of the first authority prescription, to allow for the uninterrupted completion of the six months initial treatment course. The Department of Human Services will contact prescribers prior to dispatch of the second authority prescription to confirm the tablet strength required for the patient. **Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.1.2 Treatment Phase: Initial 2 (new patients) – entire restriction deleted

6.1.3 Treatment Phase: Initial 3 Initial 2 (change or re-commencement of therapy for all patients) - bosentan

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial ~~2~~3 (change or re-commencement of therapy for all patients)
Restriction Level / Method	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class II PAH or WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease or PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology)~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have *WHO Functional Class II PAH or WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease or PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology)~~ and whose most recent course of PBS-subsidised treatment was with a PAH agent other than this agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) two completed authority prescription forms; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form; and (3) the results of the patient's response to treatment with their last course of PBS-subsidised PAH agent. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. Response to a PAH agent is defined as follows: For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~.

	For 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 *PAH* designated *centre* ~~hospital~~. 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 *PAH* designated *centre* ~~hospital~~. Approvals for the first authority prescription will be limited to 1 month of therapy with the 62.5 mg strength tablet, with the quantity approved based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. No repeats will be authorised for this prescription. The second authority prescription may be written for either the 62.5 mg tablet or the 125 mg tablet strengths. Approvals for the second authority prescription will be limited to 1 month of treatment, with the quantity approved based on the dosage recommendations in the TGA-approved Product Information, and a maximum of 4 repeats. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted. Swapping between PAH agents: Patients can access PAH agents through the PBS according to the relevant restrictions. Once these patients are approved initial treatment with 1 of these 8 drugs, they may swap between PAH agents at any time without having to re-qualify for treatment with the alternate agent. This means that patients may commence treatment with the alternate agent, subject to that agent's restriction, irrespective of the severity of their disease at the time the application to swap therapy is submitted. It also means that no new baseline measurements will be necessary. New baselines may be submitted where the patient has failed to respond to their current treatment. Eligible patients may only swap between PAH agents if they have not failed prior PBS-subsidised treatment with that agent. For eligible patients, applications to swap between the 8 PAH agents must be made under the relevant initial treatment restriction. Patients should be assessed for response to the treatment they are ceasing at the time the application to swap therapy is being made. Patients who fail to demonstrate a response or for whom no assessment results are submitted with the application to swap therapy may not re-commence PBS-subsidised treatment with the drug they are ceasing.
Administrative Advice	**Note** Where the 62.5 mg tablet strength is required for the second authority prescription, please contact the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday) for further advice. The approved second authority prescription will be returned to the prescriber by the Department of Human Services two weeks after the date of the approval of the first authority prescription, to allow for the uninterrupted completion of the six months initial treatment course. The Department of Human Services will contact prescribers prior to dispatch of the second authority prescription to confirm the tablet strength required for the patient. **Note** Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing.

	Refer Common Administrative Advice Section 6.10.1
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.1.4 Treatment Phase: Cessation of treatment (all patients) – bosentan (5618Q, 6429J only)

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Cessation of treatment (all patients)
Restriction Level / Method:	☒Authority Required - Telephone
Clinical criteria:	Patient must have received approval for initial PBS-subsidised treatment with this agent, **AND** Patient must have not responded to prior PBS-subsidised therapy with this agent, **AND** The treatment must be for the purpose of gradual dose reduction prior to ceasing therapy, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment. Treatment beyond 1 month will not be approved.
Administrative Advice	**Note** Applications for authorisation under this criterion may be made by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Written applications for authorisation under this criterion should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.1.5 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED BOSENTAN RESTRICTIONS:

Treatment Phase: First Continuing treatment – bosentan

Treatment Phase: Subsequent Continuing treatment – bosentan

Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply – bosentan

6.2 AMBRISENTAN

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
AMBRISENTAN						
5 MG TABLET, 30 S100 HSD Public	5607D	1	0	$2732.65	Volibris®	GSK
5 MG TABLET, 30 S100 HSD Private	9648T	1	0	$2779.94		
10 MG TABLET, 30 S100 HSD Public	5608E	1	0	$2732.65		
10 MG TABLET, 30 S100 HSD PRIVATE	9649W	1	0	$2779.94		

The revised PBS restrictions for ambrisentan have five treatment phases instead of the previous six treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions - Treatment Phases	Draft Revised Restrictions Treatment Phases	Restriction Location within this Document
Initial 1 (new patients)	Initial 1 (new patients)	6.2.1
Initial 2 (new patients)	~~Initial 2 (new patients)~~	6.2.2 (deleted)
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.2.3
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Refer 6.9.3

Amend existing/recommended listing of ambrisentan as follows:

Changes appear in *italics* and ~~strikethrough~~

6.2.1 Treatment Phase: Initial 1 (new patients)- ambrisentan

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 1 (new patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent,

	AND Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** *Patient must have WHO Functional Class II PAH, or WHO Functional Class III PAH, or WHO Functional Class IV PAH,* ~~Patient must have WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class III pulmonary arterial hypertension secondary to connective tissue disease,~~ ~~**AND**~~ ~~Patient must have a mean right atrial pressure of 8 mmHg or less as measured by right heart catheterisation (RHC); OR~~ ~~Patient must have right ventricular function assessed by echocardiography (ECHO) where a RHC cannot be performed on clinical grounds,~~ ~~**AND**~~ ~~Patient must have failed to respond to 6 or more weeks of appropriate vasodilator treatment unless intolerance or a contraindication to such treatment exists~~, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*
	  ○ *Congenital heart disease*
	  ○ *Schistosomiasis*

Prescriber Instructions	**Refer Common Prescriber instructions A Section 6.10.2**
Administrative Advice	**Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.2.2 Treatment Phase: ~~*Initial 2 (new patients)*~~ – entire restriction deleted

6.2.3 Treatment Phase: Initial ~~3~~ *2* (change or re-commencement of therapy for all patients) – ambrisentan

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial *2*~~3~~ (change or re-commencement of therapy for all patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class II PAH or WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have *WHO Functional Class II PAH or WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and whose most recent course of PBS-subsidised treatment was with a PAH agent other than this agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	**Refer Common Prescriber instructions B Section 6.10.3**
Administrative Advice	**Note** Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing. **Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.2.4 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED AMBRISENTAN RESTRICTIONS:

Treatment Phase: First Continuing treatment – Ambrisentan

Treatment Phase: Subsequent Continuing treatment – Ambrisentan

Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply– Ambrisentan

6.3 MACITENTAN

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
MACITENTAN 10MG TABLET S100 HSD public hospital 10MG TABLET S100 HSD PRIVATE HOSPITAL	 10136L 10134J	 1 1	 0 0	 $2876.47 $2923.76	Opsumit®	Actelion

The revised PBS restrictions for macitentan have five treatment phases instead of the previous six treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions - Treatment Phases	Draft Revised Restrictions Treatment Phases	Restriction Location within this Document
Initial 1 (new patients)	Initial 1 (new patients)	6.3.1
Initial 2 (new patients)	~~Initial 2 (new patients)~~	6.3.2 (deleted)
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.3.3
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Refer 6.9.3

Amend existing/recommended listing of macitentan as follows:

Changes appear in *italics* and ~~strikethrough~~

6.3.1 Treatment Phase: Initial 1 (new patients) - macitentan

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Treatment Phase: Initial 1 (new patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent, **AND**

	Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** *Patient must have WHO Functional Class II PAH, or WHO Functional Class III PAH, or WHO Functional Class IV PAH,* ~~Patient must have WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class III pulmonary arterial hypertension secondary to connective tissue disease,~~ ~~**AND**~~ ~~Patient must have a mean right atrial pressure of 8 mmHg or less as measured by right heart catheterisation (RHC); OR~~ ~~Patient must have right ventricular function assessed by echocardiography (ECHO) where a RHC cannot be performed on clinical grounds,~~ ~~**AND**~~ ~~Patient must have failed to respond to 6 or more weeks of appropriate vasodilator treatment unless intolerance or a contraindication to such treatment exists,~~ **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*
	  ○ *Congenital heart disease*
	  ○ *Schistosomiasis*

Prescriber Instructions	**Refer Common Prescriber instructions A Section 6.10.2**
Administrative Advice	**Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.3.2 Treatment Phase: ~~Initial 2 (new patient)~~ – entire restriction deleted

6.3.3 Treatment Phase: Initial ~~3~~ *2* (change or re-commencement for all patients) – macitentan

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial ~~3~~ *2* (change or re-commencement of therapy for all patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class II PAH or WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease or PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology)~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have *WHO Functional Class II PAH or WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease or PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology)~~ and whose most recent course of PBS-subsidised treatment was with a PAH agent other than this agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	**Refer Common Prescriber instructions B Section 6.10.3 with the following change** A maximum of 5 repeats may be ~~authorised~~ *requested*
Administrative Advice	**Note** Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing. **Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.3.4 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED MACITENTAN RESTRICTIONS:

Treatment Phase: First Continuing treatment - macitentan

Treatment Phase: Subsequent Continuing treatment – macitentan

Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply– macitentan

6.4 SILDENAFIL

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
SILDENAFIL 20mg tablet S100 HSD Public 20MG TABLET S100 HSD PRIVATE	 9547L 9605M	 1 1	 0 0	 $254.31 $271.77	Revatio® and other brands	Pfizer Australia and other manufacturers

The revised PBS restrictions for sildenafil have five treatment phases instead of the previous six treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions - Treatment Phases	Draft Revised Restrictions Treatment Phases	Restriction Location within this Document
Initial 1 (new patients)	Initial 1 (new patients)	6.4.1
Initial 2 (new patients)	~~Initial 2 (new patients)~~	6.4.2 (deleted)
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.4.3
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Refer 6.9.3

Amend existing/recommended listing of sildenafil as follows:

Changes appear in *italics* and ~~strikethrough~~

6.4.1 Treatment Phase: Initial 1 (new patients) – sildenafil

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 1 (new patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent,

	AND Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** Patient must have *WHO Functional Class II PAH, or WHO Functional Class III PAH,* ~~Patient must have WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class III pulmonary arterial hypertension secondary to connective tissue disease,~~ ~~**AND**~~ ~~Patient must have a mean right atrial pressure of 8 mmHg or less as measured by right heart catheterisation (RHC); OR~~ ~~Patient must have right ventricular function assessed by echocardiography (ECHO) where a RHC cannot be performed on clinical grounds,~~ ~~**AND**~~ ~~Patient must have failed to respond to 6 or more weeks of appropriate vasodilator treatment unless intolerance or a contraindication to such treatment exists,~~ **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*
	  ○ *Congenital heart disease*
	  ○ *Schistosomiasis*

Prescriber Instructions	**Refer Common Prescriber instructions A Section 6.10.2**
Administrative Advice	**Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.4.2 Treatment Phase: ~~Initial 2 (new patients)~~ – entire restriction deleted

6.4.3 Treatment Phase: Initial ~~3~~ *2* (change or re-commencement of therapy for all patients) - sildenafil

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Treatment Phase: Initial 2~~3~~ (change or re-commencement of therapy for all patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class II or WHO Functional Class III PAH* ~~WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have *WHO Functional Class II or WHO Functional Class III PAH* ~~WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and whose most recent course of PBS-subsidised treatment was with a PAH agent other than this agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	**Refer Common Prescriber instructions B Section 6.10.3**
Administrative Advice	**Note** Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing. **Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.4.4 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED SILDENAFIL RESTRICTIONS:

Treatment Phase: First Continuing treatment - sildenafil

Treatment Phase: Subsequent Continuing treatment – sildenafil

Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply-– sildenafil

6.5 TADALAFIL

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
TADALAFIL						
20MG TABLET S100 HSD Public	1308W	1	0	$796.60	Adcirca®	Eli Lilly Australia
20MG TABLET S100 HSD PRIVATE	1304P	1	0	$835.75	Adcirca®	

The revised PBS restrictions for tadalafil have five treatment phases instead of the previous six treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions - Treatment Phases	Draft Revised Restrictions Treatment Phases	Restriction Location within this Document
Initial 1 (new patients)	Initial 1 (new patients)	6.5.1
Initial 2 (new patients)	~~Initial 2 (new patients)~~	6.5.2 (deleted)
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.5.3
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Refer 6.9.3

Amend existing/recommended listing of tadalafil as follows:

Changes appear in *italics* and ~~strikethrough~~

6.5.1 Treatment Phase: Initial 1 (new patients) - tadalafil

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 1 (new patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent, **AND** Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~,

	AND Patient must have *WHO Functional Class II PAH, or WHO Functional Class III PAH,* ~~Patient must have WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class III pulmonary arterial hypertension secondary to connective tissue disease,~~ ~~**AND**~~ ~~Patient must have a mean right atrial pressure of 8 mmHg or less as measured by right heart catheterisation (RHC); OR~~ ~~Patient must have right ventricular function assessed by echocardiography (ECHO) where a RHC cannot be performed on clinical grounds,~~ ~~**AND**~~ ~~Patient must have failed to respond to 6 or more weeks of appropriate vasodilator treatment unless intolerance or a contraindication to such treatment exists,~~ **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*
	  ○ *Congenital heart disease*
	  ○ *Schistosomiasis*

Prescriber Instructions	**Refer Common Prescriber instructions A Section 6.10.2**
Administrative Advice	**Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.5.2 Treatment Phase: ~~Initial 2 (new patients)~~ – entire restriction deleted

6.5.3 Treatment Phase: Initial ~~3~~ *2* (change or re-commencement of therapy for all patients) - tadalafil

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Treatment Phase: Initial 2~~3~~ (change or re-commencement of therapy for all patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class II or WHO Functional Class III PAH* ~~WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have *WHO Functional Class II or WHO Functional Class III PAH* ~~WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and whose most recent course of PBS-subsidised treatment was with a PAH agent other than this agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	**Refer Common Prescriber instructions B Section 6.10.3**
Administrative Advice	**Note** Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing. **Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.5.4 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED TADALAFIL RESTRICTIONS:

Treatment Phase: First Continuing treatment – tadalafil

Treatment Phase: Subsequent Continuing treatment – tadalafil

Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply-–tadalafil

6.6 EPOPROSTENOL

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
EPOPROSTENOL						
injection 500mg S100 HSD Public	10130E	1	0	$33.28	Veletri®	Actelion Pharmaceuticals Australia
injection 500mg S100 HSD Private	10111E	1	0	$43.90		
injection 1.5mg S100 HSD Public	10117L	1	0	$66.55		
injection 1.5mg S100 HSD Private	10129D	1	0	$77.84		
injection & diluent 500mg S100 HSD	11090Q	1	0	$33.28	Flolan®	GlaxoSmithKline Australia
injection & diluent 500mg S100 HSD Private	11069N	1	0	$43.90		
injection & diluent 1.5mg S100 HSD Public	11065J	1	0	$66.55		
injection & diluent 1.5mg S100 HSD Private	11082G	1	0	$77.84		

The revised PBS restrictions for epoprostenol retain five treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions - Treatment Phases	Draft Revised Restrictions Treatment Phases	Restriction Location within this Document
Initial 1 (new patients)	Initial 1 (new patients)	6.6.1
Initial 2 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.6.2
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	6.6.3

Amend existing/recommended listing of epoprostenol as follows:

Changes appear in *italics* and ~~strikethrough~~

6.6.1 Treatment Phase: Initial 1 (new patient) - epoprostenol

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)

Treatment phase:	Treatment Phase: Initial 1 (new patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent, **AND** Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** Patient must have WHO Functional Class IV *PAH* ~~idiopathic pulmonary arterial hypertension (iPAH), or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class IV pulmonary arterial hypertension secondary to connective tissue disease,~~ **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*
	  ○ *Congenital heart disease*
	  ○ *Schistosomiasis*

Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form which includes results from the three tests below, where available: (i) RHC composite assessment; and (ii) ECHO composite assessment; and (iii) 6 Minute Walk Test (6MWT); and (3) a signed patient acknowledgement. ~~Idiopathic pulmonary arterial hypertension, anorexigen-induced pulmonary arterial hypertension, hereditable pulmonary arterial hypertension, drug-induced pulmonary arterial hypertension, pulmonary arterial hypertension secondary to connective tissue disease including scleroderma, or pulmonary arterial hypertension associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology) are defined as follows:~~ *PAH (WHO Group I pulmonary hypertension) is defined as follows:*

	(i) mean pulmonary artery pressure (mPAP) greater than *or equal to* 25 mmHg at rest and pulmonary artery wedge pressure (PAWP) less than *or equal to* 15 mmHg; or (ii) where a right heart catheter (RHC) cannot be performed on clinical grounds, right ventricular systolic pressure (RVSP), assessed by echocardiography (ECHO), greater than 40 mmHg, with normal left ventricular function. ~~Test requirements to establish baseline for initiation of treatment are as follows:~~ The first written application for PBS-subsidised treatment with the first PAH agent should be accompanied by the results of a right heart catheter (RHC) composite assessment plus an echocardiograph (ECHO) composite assessment, plus a 6 minute walk test (6MWT) to establish the patient's baseline measurements. Where it is not possible to perform all 3 tests above 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 submitted 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. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. A maximum of 5 repeats may be requested. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted.
Administrative Advice	**Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.6.2 Treatment Phase: Initial 2 (change or re-commencement of therapy for all patients) - epoprostenol

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 2 (change or re-commencement of therapy for all patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have WHO Functional Class IV *PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must have received prior treatment with a PBS-subsidised PAH agent other than this agent; OR Patient must have WHO Functional Class III *PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must have failed to respond to a prior PBS-subsidised PAH agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form; and (3) the results of the patient's response to treatment with their last course of PBS-subsidised PAH agent; and (4) for WHO Functional Class III patients, where this is the first application for this agent, assessment details of the PBS-subsidised PAH agent they have failed to respond to. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. Response to a PAH agent is defined as follows: For 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 *PAH* designated *centre* ~~hospital~~.

	For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~. 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 *PAH* designated *centre* ~~hospital~~. The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. A maximum of 5 repeats may be requested. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted. Swapping between PAH agents: Patients can access PAH agents through the PBS according to the relevant restrictions. Once these patients are approved initial treatment with 1 of these 8 drugs, they may swap between PAH agents at any time without having to re-qualify for treatment with the alternate agent. This means that patients may commence treatment with the alternate agent, subject to that agent's restriction, irrespective of the severity of their disease at the time the application to swap therapy is submitted. It also means that no new baseline measurements will be necessary. New baselines may be submitted where the patient has failed to respond to their current treatment. Eligible patients may only swap between PAH agents if they have not failed prior PBS-subsidised treatment with that agent. For eligible patients, applications to swap between the 8 PAH agents must be made under the relevant initial treatment restriction. Patients should be assessed for response to the treatment they are ceasing at the time the application to swap therapy is being made. Patients who fail to demonstrate a response or for whom no assessment results are submitted with the application to swap therapy may not re-commence PBS-subsidised treatment with the drug they are ceasing.
Administrative Advice	**Note** Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing. **Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.6.3 Treatment Phase: Initial 1 (new patients) or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply - Epoprostenol

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 1 (new patients) or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply
Restriction Level / Method:	☒Authority Required – Telephone
Clinical criteria:	Patient must have received insufficient therapy with this agent under the Initial 1 (new patients) restriction to complete a maximum of six months of treatment; OR Patient must have received insufficient therapy with this agent under the Initial 2 (change or re-commencement of therapy for all patients) restriction to complete a maximum of six months of treatment; OR Patient must have received insufficient therapy with this agent under the First Continuing treatment restriction to complete a maximum of six months of treatment, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition, **AND** The treatment must provide no more than the balance of up to six months treatment available under one of the above restrictions.
Administrative Advice	**Note** Applications for authorisation under this criterion may be made by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Written applications for authorisation under this criterion should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.6.4 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED EPOPROSTENOL RESTRICTIONS:

Treatment Phase First Continuing treatment – epoprostenol

Treatment Phase: Subsequent Continuing treatment – epoprostenol

6.7 ILOPROST

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
ILOPROST 20 microgram/2 mL inhalation solution, 30 x 2 mL ampoules S100 HSD Public	5751Q	1	0	$367.99	Ventavis®	Bayer Australia
20 microgram/2 mL inhalation solution, 30 x 2 mL ampoules S100 HSD Private	6456T	1	0	$390.00		

The revised PBS restrictions for iloprost have five treatment phases instead of the previous six treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions – Treatment Phases	Draft Revised Restrictions Treatment Phases	Restriction Location within this Document
Initial 1 (new patients)	~~Initial 1 (new patients)~~	6.7.1 (deleted)
Initial 2 (new patients)	Initial 1 (new patients)	6.7.2
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.7.3
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Refer 6.9.3

Amend existing/recommended listing of iloprost as follows:

Changes appear in *italics* and ~~strikethrough~~

6.7.1 Treatment Phase: ~~Initial 1 (new patients)~~ – entire restriction deleted

6.7.2 Treatment Phase Initial ~~2~~ *1* (new patients) – iloprost

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial ~~2~~ *1* (new patients)

Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent, **AND** Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** Patient must have WHO Functional Class III ~~drug-induced~~ *drug and toxins induced* PAH ~~and a mean right atrial pressure greater than 8 mmHg, as measured by right heart catheterisation (RHC)~~; OR ~~Patient must have WHO Functional Class III drug-induced PAH with right ventricular function assessed by echocardiography (ECHO) where a RHC cannot be performed on clinical grounds; OR~~ Patient must have WHO Functional Class IV *PAH,* ~~idiopathic pulmonary arterial hypertension (iPAH), or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class IV pulmonary arterial hypertension secondary to connective tissue disease; OR~~ ~~Patient must have WHO Functional Class IV drug-induced PAH,~~ **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*
	  ○ *Congenital heart disease*
	  ○ *Schistosomiasis*

Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form which includes results from the three tests below, where available: (i) RHC composite assessment; and (ii) ECHO composite assessment; and (iii) 6 Minute Walk Test (6MWT); and (3) a signed patient acknowledgement. ~~Idiopathic pulmonary arterial hypertension, anorexigen-induced pulmonary arterial hypertension, hereditable pulmonary arterial hypertension, drug-~~

	~~induced pulmonary arterial hypertension, pulmonary arterial hypertension secondary to connective tissue disease including scleroderma, or pulmonary arterial hypertension associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology) are defined as follows:~~ *PAH is defined as follows:* (i) mean pulmonary artery pressure (mPAP) greater than *or equal to* 25 mmHg at rest and pulmonary artery wedge pressure (PAWP) less than *or equal to* 15 mmHg; or (ii) where a right heart catheter (RHC) cannot be performed on clinical grounds, right ventricular systolic pressure (RVSP), assessed by echocardiography (ECHO), greater than 40 mmHg, with normal left ventricular function. ~~Test requirements to establish baseline for initiation of treatment are as follows:~~ The first written application for PBS-subsidised treatment with the first PAH agent should be accompanied by the results of a right heart catheter (RHC) composite assessment plus an echocardiograph (ECHO) composite assessment, plus a 6 minute walk test (6MWT) to establish the patient's baseline measurements. Where it is not possible to perform all 3 tests above 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 submitted 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. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. A maximum of 5 repeats may be requested. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat.
Administrative Advice	The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent.

	PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted.
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.7.3 Treatment Phase: Initial ~~*3*~~ *2* (change or re-commencement of therapy for all patients) - iloprost

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Episodicity:	
Severity:	
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 2~~3~~ (change or re-commencement of therapy for all patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class III drug and toxin induced PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease or drug-induced PAH~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have *WHO Functional Class IV PAH* ~~WHO Functional Class IV idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must have received prior treatment with a PBS-subsidised PAH agent other than this agent; OR Patient must have WHO Functional Class III *PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease~~ and must have failed to respond to a prior PBS-subsidised PAH agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form; and (3) the results of the patient's response to treatment with their last course of PBS-subsidised PAH agent; and (4) for WHO Functional Class III patients, where this is the first application for this agent, assessment details of the PBS-subsidised PAH agent they have failed to respond to. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application. The test results provided must not be more than 2 months old at the time of application. Response to a PAH agent is defined as follows: For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~. 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 *PAH* designated *centre* ~~hospital~~. The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. A maximum of 5 repeats may be requested. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted. Swapping between PAH agents: Patients can access PAH agents through the PBS according to the relevant restrictions. Once these patients are approved initial treatment with 1 of these 8 drugs, they may swap between PAH agents at any time without having to re-qualify for treatment with the alternate agent. This means that patients may commence treatment with the alternate agent, subject to that agent's restriction, irrespective of the severity of their disease at the time the application to swap therapy is submitted. It also means that no new baseline measurements will be necessary. New baselines may be submitted where the patient has failed to respond to their current treatment. Eligible patients may only swap between PAH agents if they have not failed prior PBS-subsidised treatment with that agent. For eligible patients, applications to swap between the 8 PAH agents must be made under the relevant initial treatment restriction. Patients should be assessed for response to the treatment they are ceasing at the time the application to swap therapy is being made. Patients who fail to demonstrate a response or for whom no assessment results are submitted with the application to swap therapy may not re-commence PBS-subsidised treatment with the drug they are ceasing.
Administrative Advice	**Note**

	Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing. **Refer Common Administrative Advice Section 6.10.1** **Note** Special Pricing Arrangements apply.
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.7.4 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED ILOPROST RESTRICTIONS:

Treatment Phase: First Continuing treatment – iloprost

Treatment Phase: Subsequent Continuing treatment – iloprost

Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply-iloprost

6.8 RIOCIGUAT

Name, Restriction, Manner of administration and form	Item Number	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
RIOCIGUAT						
tablet 500 microgram, 42, S100 HSD Public	11040C	1	0	$1717.71	Adempas®	Bayer Australia
tablet 500 microgram, 42, S100 HSD Private	11031N	1	0	$1765.00		
tablet 500 microgram, 84, S100 HSD Public	11059C	1	0	$3435.42		
tablet 500 microgram, 84, S100 HSD Private	11058B	1	0	$3482.71		
tablet 1mg, 42, S100 HSD Public	11054T	1	0	$1717.71		
tablet 1mg, 42, S100 HSD Private	11028K	1	0	$1765.00		
tablet 1mg, 84, S100 HSD Public	11053R	1	0	$3435.42		
tablet 1mg, 84, S100 HSD Private	11060D	1	0	$3482.71		
tablet 1.5mg, 42, S100 HSD Public	11047K	1	0	$1717.71		
tablet 1.5mg, 42, S100 HSD Private	11046J	1	0	$1765.00		
tablet 1.5mg, 84, S100 HSD Public	11048L	1	0	$3435.42		
tablet 1.5mg, 84, S100 HSD Private	11061E	1	0	$3482.71		
tablet 2mg, 42, S100 HSD Public	11038Y	1	0	$1717.71		
tablet 2mg, 42, S100 HSD Private	11045H	1	0	$1765.00		
tablet 2mg, 84, S100 HSD Public	11039B	1	0	$3435.42		
tablet 2mg, 84, S100 HSD Private	11030M	1	0	$3482.71		
tablet 2.5mg, 42, S100 HSD Public	11057Y					
tablet 2.5mg, 42, S100 HSD Private	11052Q					
tablet 2.5mg, 84, S100 HSD Public	11024F					
tablet 2.5mg, 84, S100 HSD Private	11035T					

The revised PBS restrictions for riociguat have five treatment phases instead of the previous six treatment phases. The locations of the revised restrictions within this section are summarised in the following table.

Current Restrictions - Treatment Phases	Draft Revised Restrictions Treatment Phases	Restriction Location within this Document

Initial 1 (new patients)	Initial 1 (new patients)	6.8.1
Initial 2 (new patients)	~~Initial 2 (new patients)~~	6.8.2 (deleted)
Initial 3 (change or re-commencement of therapy for all patients)	Initial 2 (change or re-commencement of therapy for all patients)	6.8.3
First Continuing treatment	First Continuing treatment	Refer 6.9.1
Subsequent Continuing treatment	Subsequent Continuing treatment	Refer 6.9.2
Initial 1 (new patients) or Initial 2 (new patients) or Initial 3 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Initial 1 or Initial 2 (change or re-commencement of therapy for all patients) or First Continuing treatment - Balance of supply	Refer 6.9.3

Amend existing/recommended listing of riociguat as follows:

Changes appear in *italics* and ~~strikethrough~~

6.8.1 Treatment Phase: Initial 1 (new patients) - riociguat

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Treatment Phase: Initial 1 (new patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have received prior PBS-subsidised treatment with a pulmonary arterial hypertension (PAH) agent, **AND** Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** *Patient must have WHO Functional Class III PAH or WHO Functional Class IV PAH,* ~~Patient must have WHO Functional Class III idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH; OR~~ ~~Patient must have WHO Functional Class III pulmonary arterial hypertension secondary to connective tissue disease,~~ ~~**AND**~~ ~~Patient must have a mean right atrial pressure of 8 mmHg or less as measured by right heart catheterisation (RHC); OR~~ ~~Patient must have right ventricular function assessed by echocardiography (ECHO) where a RHC cannot be performed on clinical grounds,~~ ~~**AND**~~

	~~Patient must have failed to respond to 6 or more weeks of appropriate vasodilator treatment unless intolerance or a contraindication to such treatment exists,~~ **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.

Definitions	*PAH (WHO Group 1 pulmonary hypertension) currently includes the following subtypes:*
	• *Idiopathic PAH*
	• *Heritable PAH*
	  ○ *BMPR2 mutation*
	  ○ *ALK-1, ENG, SMAD9, CAV1, KCNK3 mutations*
	  ○ *Other mutations*
	• *Drugs and toxins induced PAH*
	• *PAH associated with:*
	  ○ *Connective tissue disease*
	  ○ *Human immunodeficiency virus (HIV) infection*
	  ○ *Portal hypertension*
	  ○ *Congenital heart disease*
	  ○ *Schistosomiasis*

Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) completed authority prescription forms sufficient for dose titration; and (2) a completed Pulmonary Arterial Hypertension Initial PBS Authority Application – Supporting Information form which includes results from the three tests below, where available: (i) RHC composite assessment; and (ii) ECHO composite assessment; and (iii) 6 Minute Walk Test (6MWT); and (3) a signed patient acknowledgement. ~~Idiopathic pulmonary arterial hypertension, anorexigen-induced pulmonary arterial hypertension, hereditable pulmonary arterial hypertension, drug-induced pulmonary arterial hypertension, pulmonary arterial hypertension secondary to connective tissue disease including scleroderma, or pulmonary arterial hypertension associated with a congenital systemic to pulmonary shunt (including Eisenmenger's physiology) are defined as follows:~~ *PAH (WHO Group I pulmonary hypertension) is defined as follows:* (i) mean pulmonary artery pressure (mPAP) greater than *or equal to* 25 mmHg at rest and pulmonary artery wedge pressure (PAWP) less than *or equal to* 15 mmHg; or (ii) where a right heart catheter (RHC) cannot be performed on clinical grounds, right ventricular systolic pressure (RVSP), assessed by echocardiography (ECHO), greater than 40 mmHg, with normal left ventricular function. ~~Test requirements to establish baseline for initiation of treatment are as follows:~~ The first written application for PBS-subsidised treatment with the first PAH agent should be accompanied by the results of a right heart catheter (RHC) composite assessment plus an echocardiograph (ECHO) composite assessment, plus a 6 minute walk test (6MWT) to establish the patient's baseline measurements. Where it is not possible to perform all 3 tests above 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 submitted 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. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. ~~Details of prior vasodilator treatment, including the dose and duration of treatment, must be provided at the time of application. Where the patient has an adverse event to a vasodilator or where vasodilator treatment is contraindicated, details of the nature of the adverse event or contraindication according to the Therapeutic Goods Administration (TGA) approved Product Information must also be provided with the application.~~ ~~Response to prior vasodilator treatment is defined as follows:~~ ~~For patients with 2 or more baseline tests, response to treatment is defined as 2 or more tests demonstrating stability or improvement of disease, as assessed by a physician from a designated hospital.~~ ~~For 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 hospital.~~ ~~For 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 hospital.~~ ~~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 hospital.~~ Approvals for prescriptions for dose titration will provide sufficient quantity for dose titrations by 0.5 mg increments at 2-week intervals to achieve up to a maximum of 2.5 mg three times daily based on the dosage recommendations for initiation of treatment in the TGA-approved Product Information. No repeats will be authorised for these prescriptions. Approvals for subsequent authority prescription will be limited to 1 month of treatment, with the quantity approved based on the dosage recommendations in the TGA-approved Product Information, and a maximum of 4 repeats. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat.

	PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted.
Administrative Advice	**Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.8.2 Treatment Phase~~: Initial 2 (new patients~~) – entire restriction deleted

6.8.3 Treatment Phase: ~~Initial 3~~ *2* (change or re-commencement of therapy for all patients) - riociguat

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 2~~3~~ (change or re-commencement of therapy for all patients)
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have *WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease or PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology)~~ and must wish to re-commence PBS-subsidised therapy with this agent after a break in therapy and must have demonstrated a response to their most recent course of PBS-subsidised treatment with this agent; OR Patient must have *WHO Functional Class III PAH or WHO Functional Class IV PAH* ~~idiopathic pulmonary arterial hypertension (iPAH) or anorexigen-induced PAH or hereditable PAH or PAH secondary to connective tissue disease or PAH associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology)~~ and whose most recent course of PBS-subsidised treatment was with a PAH agent other than this agent, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form; and (3) the results of the patient's response to treatment with their last course of PBS-subsidised PAH agent. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. Response to a PAH agent is defined as follows: For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~.

	For 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 *PAH* designated *centre* ~~hospital~~. 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 *PAH* designated *centre* ~~hospital~~. Approvals for prescriptions for dose titration will provide sufficient quantity for dose titrations by 0.5 mg increments at 2-week intervals to achieve up to a maximum of 2.5 mg three times daily based on the dosage recommendations for initiation of treatment in the TGA-approved Product Information. No repeats will be authorised for these prescriptions. Approvals for subsequent authority prescription will be limited to 1 month of treatment, with the quantity approved based on the dosage recommendations in the TGA-approved Product Information, and a maximum of 4 repeats. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted. Swapping between PAH agents: Patients can access PAH agents through the PBS according to the relevant restrictions. Once these patients are approved initial treatment with 1 of these 8 drugs, they may swap between PAH agents at any time without having to re-qualify for treatment with the alternate agent. This means that patients may commence treatment with the alternate agent, subject to that agent's restriction, irrespective of the severity of their disease at the time the application to swap therapy is submitted. It also means that no new baseline measurements will be necessary. New baselines may be submitted where the patient has failed to respond to their current treatment. Eligible patients may only swap between PAH agents if they have not failed prior PBS-subsidised treatment with that agent. For eligible patients, applications to swap between the 8 PAH agents must be made under the relevant initial treatment restriction. Patients should be assessed for response to the treatment they are ceasing at the time the application to swap therapy is being made. Patients who fail to demonstrate a response or for whom no assessment results are submitted with the application to swap therapy may not re-commence PBS-subsidised treatment with the drug they are ceasing.
Administrative Advice	**Note** Applications for patients who wish to swap to an alternate PAH agent should be accompanied by the previously approved authority prescription, or remaining repeats, for the treatment the patient is ceasing. **Refer Common Administrative Advice Section 6.10.1**
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.8.4 REFER SECTION 6.9 COMMON RESTRICTIONS FOR THE FOLLOWING AMENDED RIOCIGUAT RESTRICTIONS:

Treatment Phase: First Continuing treatment – riociguat

Treatment Phase: Subsequent Continuing treatment – riociguat

Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply– riociguat

6.9 COMMON RESTRICTIONS FOR BOSENTAN, AMBRISENTAN, MACITENTAN, SILDENAFIL, TADALAFIL, EPOPROSTENOL, ILOPROST AND RIOCIGUAT

The following amended restrictions are common to all PAH targeted medicines for the following treatment phases:

- First Continuing Treatment
- Subsequent Continuing Treatment
- Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply

The recommended restrictions are presented together for conciseness below.

6.9.1 Treatment Phase: First Continuing treatment

Amend existing/recommended listings of bosentan, ambrisentan, macitentan, sildenafil, tadalafil, epoprostenol, iloprost and riociguat as follows:

Changes appear in *italics* and ~~strikethrough~~

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	First Continuing treatment
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have received a PBS-subsidised initial course of treatment with this agent for this condition, **AND** Patient must have been assessed by a physician from a *PAH* designated *centre* ~~hospital~~ to have achieved a response to the PBS-subsidised initial course of treatment, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form which includes results from the three tests below, where available: (i) RHC composite assessment; and (ii) ECHO composite assessment; and (iii) 6 Minute Walk Test (6MWT). Test requirements to establish response to treatment for continuation of treatment are as follows: 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. The results of the same tests as conducted at baseline should be provided with the written First Continuing treatment application, except for patients who were able to undergo all 3 tests at baseline, and whose subsequent ECHO and 6MWT results demonstrate disease stability or improvement, in which case RHC can be omitted. In all other patients, where the same test(s) conducted at baseline cannot be performed for assessment of response on clinical grounds, a patient specific reason why the test(s) could not be conducted must be provided with the application. *Where a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application* The test results provided with the application for continuing treatment must be no more than 2 months old at the time of application. Response to a PAH agent is defined as follows: For patients with two or more baseline tests, response to treatment is defined two or more tests demonstrating stability or improvement of disease, as assessed by a physician from a *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~. For patients aged less than 18 years, response to treatment is defined at least one of the baseline tests demonstrating stability or improvement of disease, as assessed by a physician from a *PAH* designated *centre* ~~hospital~~. The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. A maximum of 5 repeats will be authorised. An application for First Continuing treatment with a PAH agent should be made prior to the completion of the Initial 6 month treatment course to ensure continuity for those patients who respond to treatment, as assessed by the treating physician. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted.

Administrative Advice	**Note** Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001 **Note** Refer to the Department of Human Services website at www.humanservices.gov.au for a list of *PAH* designated *centres* ~~hospitals~~.
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.9.2 Treatment Phase: Subsequent Continuing treatment

Amend existing/recommended listings of bosentan, ambrisentan, macitentan, sildenafil, tadalafil, epoprostenol, iloprost and riociguat as follows. Note for riogiguat, the following is an addition:

Written applications for authorisation under this criterion should be forwarded to:

Department of Human Services

Complex Drugs

Reply Paid 9826

HOBART TAS 7001:

Changes appear in *italics* and ~~strikethrough~~

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Subsequent Continuing treatment
Restriction Level / Method:	☒Authority Required - Telephone
Clinical criteria:	Patient must have received a PBS-subsidised treatment under First Continuing treatment with this agent for this condition; OR Patient must have previously received PBS-subsidised treatment under this criteria with this agent for this condition, **AND**

	Patient must have been assessed by a physician at a *PAH* designated *centre* ~~hospital~~, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition.
Prescriber Instructions	The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. A maximum of 5 repeats will be authorised. An application for Subsequent Continuing treatment with a PAH agents should be made prior to the completion of the First Continuing treatment course to ensure continuity of treatment. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat.
Administrative Advice	**Note** Applications for authorisation under this criterion may be made by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Written applications for authorisation under this criterion should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001 **Note** Refer to the Department of Human Services website at www.humanservices.gov.au for a list of *PAH* designated *centres* ~~hospitals~~.
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy

6.9.3 Treatment Phase: Initial 1 (new patients) or Initial 2 (~~new patients~~ change or re-commencement of therapy for all patients) or ~~Initial 3 change or re-commencement of therapy for all patients~~ First Continuing treatment - Balance of supply –

Amend existing/recommended listings of bosentan, ambrisentan, macitentan, sildenafil, tadalafil, iloprost and riociguat as follows.

Note: excludes epoprostenol. Refer to restriction under 6.6.3

Note: for riogiguat, the following is an addition:

Written applications for authorisation under this criterion should be forwarded to:

Department of Human Services

Complex Drugs

Reply Paid 9826

HOBART TAS 7001

Changes appear in *italics* and ~~strikethrough~~

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Condition:	Pulmonary arterial hypertension (PAH)
PBS Indication:	Pulmonary arterial hypertension (PAH)
Treatment phase:	Initial 1 *(new patients)* or Initial 2 (~~new patients~~ *change or re-commencement of therapy for all patients*) or ~~Initial 3 (change or re-commencement of therapy for all patients) or~~ First Continuing treatment - Balance of supply
Restriction Level / Method:	☒Authority Required - Telephone
Clinical criteria:	Patient must have received insufficient therapy with this agent under the Initial 1 (new patients) restriction to complete a maximum of six months of treatment; OR Patient must have received insufficient therapy with this agent under the Initial 2 (~~new patients~~ *change or re-commencement of therapy for all patients*) restriction to complete a maximum of six months of treatment; OR ~~Patient must have received insufficient therapy with this agent under the Initial 3 (change or re-commencement of therapy for all patients) restriction to complete a maximum of six months of treatment; OR~~ Patient must have received insufficient therapy with this agent under the First Continuing treatment restriction to complete a maximum of six months of treatment, **AND** The treatment must be the sole PBS-subsidised PAH agent for this condition, **AND** The treatment must provide no more than the balance of up to six months treatment available under one of the above restrictions.
Administrative Advice	**Note** Applications for authorisation under this criterion may be made by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

	Written applications for authorisation under this criterion should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001
Cautions	This is a category X drug and must not be given to pregnant women. Pregnancy must be avoided during treatment and for at least 3 months following cessation of therapy.

6.10 Common Administrative Advice and Prescriber Instructions

6.10.1 Common Administrative Advice

This Administrative Advice is referenced in the PBS restrictions for PAH medicines as follows:

- Bosentan (refer sections 6.1.1, 6.1.3)
- Ambrisentan (refer sections 6.2.1, 6.2.3)
- Macitentan (refer sections 6.3.1, 6.3.3)
- Sildenafil (refer sections 6.4.1, 6.4.3)
- Tadalafil (refer sections 6.5.1, 6.5.3)
- Epoprostenol (refer sections 6.6.1, 6.6.2)
- Iloprost (refer sections 6.7.3)
- Riociguat (refer sections 6.8.1, 6.8.3)

Changes appear in *italics* and ~~strikethrough~~

Administrative Advice	**Note** Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au Applications for authority to prescribe should be forwarded to: Department of Human Services Prior Written Approval of Complex Drugs Reply Paid 9826 HOBART TAS 7001 **Note** Refer to the Department of Human Services website at www.humanservices.gov.au for a list of *PAH* designated *centres* ~~hospitals~~.

6.10.2 Common Prescriber instructions A

This prescriber instruction is referenced in the Treatment Phase: Initial 1 PBS restriction for the following PAH medicines: ambrisentan (refer section 6.2.1), macitentan (refer section 6.3.1), sildenafil (refer section 6.4.1), tadalafil (refer section 6.5.1).

Changes appear in *italics* and ~~strikethrough~~

Prescriber Instructions	Applications for authorisation must be in writing and must include:

	(1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form which includes results from the three tests below, where available: (i) RHC composite assessment; and (ii) ECHO composite assessment; and (iii) 6 Minute Walk Test (6MWT); and (3) a signed patient acknowledgement. ~~Idiopathic pulmonary arterial hypertension, anorexigen-induced pulmonary arterial hypertension, hereditable pulmonary arterial hypertension, drug-induced pulmonary arterial hypertension, pulmonary arterial hypertension secondary to connective tissue disease including scleroderma, or pulmonary arterial hypertension associated with a congenital systemic-to-pulmonary shunt (including Eisenmenger's physiology) are defined as follows:~~ *PAH (WHO Group I pulmonary hypertension) is defined as follows:* (i) mean pulmonary artery pressure (mPAP) greater than *or equal to* 25 mmHg at rest and pulmonary artery wedge pressure (PAWP) less than *or equal to* 15 mmHg; or (ii) where a right heart catheter (RHC) cannot be performed on clinical grounds, right ventricular systolic pressure (RVSP), assessed by echocardiography (ECHO), greater than 40 mmHg, with normal left ventricular function. ~~Test requirements to establish baseline for initiation of treatment are as follows:~~ The first written application for PBS-subsidised treatment with the first PAH agent should be accompanied by the results of a right heart catheter (RHC) composite assessment plus an echocardiograph (ECHO) composite assessment, plus a 6 minute walk test (6MWT) to establish the patient's baseline measurements. Where it is not possible to perform all 3 tests above 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 submitted 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. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application.* The test results provided must not be more than 2 months old at the time of application. ~~Details of prior vasodilator treatment, including the dose and duration of treatment, must be provided at the time of application. Where the patient has an adverse event to a vasodilator or where vasodilator treatment is contraindicated, details of the nature of the adverse event or contraindication according to the Therapeutic Goods~~

	~~Administration (TGA) approved Product Information must also be provided with the application.~~ ~~Response to prior vasodilator treatment is defined as follows:~~ ~~For patients with 2 or more baseline tests, response to treatment is defined as 2 or more tests demonstrating stability or improvement of disease, as assessed by a physician from a designated hospital.~~ ~~For 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 hospital.~~ ~~For 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 hospital.~~ ~~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 hospital.~~ The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the TGA-approved Product Information. A maximum of 5 repeats may be requested. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted.

6.10.3 Common Prescriber instructions B

This prescriber instruction is referenced in the Treatment Phase: Initial ~~3~~ 2 (change/re-commencement) PBS restriction for the following PAH medicines: ambrisentan (refer section 6.2.3), macitentan (refer section 6.3.3), sildenafil (refer section 6.4.3), tadalafil (refer section 6.5.3)

Changes appear in *italics* and ~~strikethrough~~

Prescriber Instructions	Applications for authorisation must be in writing and must include: (1) a completed authority prescription form; and (2) a completed Pulmonary Arterial Hypertension PBS Authority Application - Supporting Information form; and (3) the results of the patient's response to treatment with their last course of PBS-subsidised PAH agent. Where fewer than 3 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 a RHC cannot be performed on clinical grounds, confirmation of the reason(s) must be provided by a second cardiologist with expertise in the management of PAH or PAH physician with the authority application. The test results provided must not be more than 2 months old at the time of application. Response to a PAH agent is defined as follows: For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~. For 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 *PAH* designated *centre* ~~hospital~~. 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 *PAH* designated *centre* ~~hospital~~. The maximum quantity authorised will be limited to provide sufficient supply for 1 month of treatment, based on the dosage recommendations in the Therapeutic Goods Administration (TGA) approved Product Information. A maximum of 5 repeats may be requested. The assessment of the patient's response to the initial 6 month course of treatment should be made following the preceding 5 months of treatment, in order to allow sufficient time for a response to be demonstrated. Patients who fail to demonstrate a response to PBS-subsidised treatment with this agent at the time where an assessment is required must cease PBS-subsidised therapy with this agent. The term 'PAH agents' refers to bosentan monohydrate, iloprost trometamol, epoprostenol sodium, sildenafil citrate, ambrisentan, tadalafil, macitentan, and riociguat. PAH agents are not PBS-subsidised for patients with pulmonary hypertension secondary to interstitial lung disease associated with connective tissue disease, where the total lung capacity is less than 70% of predicted. Swapping between PAH agents: Patients can access PAH agents through the PBS according to the relevant restrictions. Once these patients are approved initial treatment with 1 of these 8 drugs, they may swap between PAH agents at any time without having to re-qualify for treatment with the alternate agent. This means that patients may commence treatment with the alternate agent, subject to that agent's restriction, irrespective of the severity of their disease at the time the application to swap therapy is submitted. It also means that no new baseline measurements will be necessary. New baselines may be submitted where the patient has failed to respond to their current treatment. Eligible patients may only swap between PAH agents if they have not failed prior PBS-subsidised treatment with that agent. For eligible patients, applications to swap between the 8 PAH agents must be made under the relevant initial treatment restriction. Patients should be assessed for response to the treatment they are ceasing at the time the application to swap therapy is being made. Patients who fail to demonstrate a response or for whom no assessment results are submitted with the application to swap therapy may not re-commence PBS-subsidised treatment with the drug they are ceasing.