Pulmonary arterial hypertension (PAH) Stakeholder Meeting

Outcome Statement

Tuesday 12 August 2025

Attendees

Members of the Pharmaceutical Benefits Advisory Committee (PBAC), clinicians with expertise in the management of pulmonary arterial hypertension (PAH), and representatives from the Department of Health, Disability and Ageing (the Department) were in attendance.

Non-departmental attendees undertook confidentiality declarations and provided conflict of interest statements.

Purpose of meeting

At its March 2025 meeting the PBAC rejected a submission for sotatercept as add-on therapy in patients with PAH World Health Organisation (WHO) functional class (FC) II-III. The PBAC noted the requested listing raised disconnections between currently available PAH medicines on the PBS and international PAH guidelines, which in turn informs the potential clinical place of sotatercept on the PBS. The PBAC requested that the Department review the restrictions for currently listed PAH medicines regarding consistency with current clinical practice and international PAH treatment guidelines.

The PBAC Chair also requested a clinician stakeholder meeting be held to discuss therapy in WHO FC II PAH including the role of sotatercept in this PAH treatment paradigm. This is consistent with the procedure guidance for listing medicines on the PBS, which outlines who may be invited to PBAC stakeholder meetings**.**

The purpose of the meeting was to seek clinician input on issues raised by the PBAC relating to changes in guideline and consensus recommended therapy in Group I PAH including (but not limited to):

- Dual therapy in WHO FC II PAH,
- The role of sotatercept in the PAH treatment paradigm
- Ways forward to optimise cost-effective PAH management

The following points were identified as areas for discussion:

1. What proportion of PAH patients present in WHO FC I and II and how is this population treated (including non-PBS therapy)?
2. Which treatment guideline(s) (if any) do Australian PAH clinicians currently follow?
3. Is treatment approach primarily guided now by WHO FC status or by risk categorisation? Which risk categorisation tools are preferred?

4. Are PBS restrictions a barrier to optimal PAH therapy? In these cases, do patients self-fund treatment, or are there compassionate access programs available?
5. Where should sotatercept be positioned in the PAH treatment algorithm? Does the 7th World Symposium in Pulmonary Hypertension algorithm accurately reflect the optimal treatment paradigm for PAH therapy in Australia?
6. Are clinicians aware of any other new treatments on horizon/close to market?

A slideshow was presented which summarised background on the 2016-18 post-market review of PAH medicines, updates to international PAH guidelines, the PBAC's March 2025 consideration of sotatercept and clinical trials supporting the use of sotatercept (PULSAR, STELLAR, SOTERIA, ZENITH and HYPERION).

Meeting discussion

Changes to PAH treatment guidelines and gaps in PBS-subsidised therapy

- Participants noted that international PAH treatment guidelines have evolved since the Department last undertook a Post-market Review of Pulmonary Arterial Hypertension in 2016-2018. Clinicians agreed that currently, the 7th World Symposium in Pulmonary Hypertension algorithm represents best practice for the treatment of PAH in Australia.
- Clinicians noted that WHO FC status is a useful assessment, but WHO FC status in isolation is not relied upon for initiating or escalating therapy. Disease severity and prognosis varies due to individual or genetic factors that influence patient outcomes. WHO FC status also carries a bias towards older patients in terms of truly describing the patient's health status, as younger patients may be able to preserve functional class whilst simultaneously being at higher risk of mortality. A younger patient with WHO FC II status may in practice be in greater need of intensive pharmacotherapy compared to an older patient with the same WHO FC status.
- In practice, treating physicians form an overall clinical risk assessment of a patient through stratifying risk via clinical markers, investigative tests, parameters and clinical observation.
- Clinicians agreed that the emphasis with treatment is to attain and maintain a low-risk status.
- Treatment guidelines recommend dual therapy for all newly diagnosed patients classified as "not high risk" (defined as less than 20 percent risk of 1 year mortality, usually in patients with PAH and WHO FC I to III status) and therapy is modified or escalated with the goal of achieving a "low-risk" status. However, the PBS currently only allows dual therapy for patients with WHO FC III-IV status. Patients newly diagnosed with FC II status may only access PBS-subsidised monotherapy (with an endothelin receptor antagonist (ERA) or a phosphodiesterase type 5 inhibitor (PDE-5i), and patients with FC I status cannot access PBS-subsidised therapy. Treatment guidelines recommend that high risk patients (those with a greater than 20% risk of 1 year mortality) at initial presentation commence triple therapy and consider assessment for lung transplant.
- Clinicians agreed that all newly diagnosed patients with PAH should have access to at least dual therapy (ERA in combination with PDE-5i), noting the addition of a PDE-5i to an ERA

often adds significant improvement with minimal adverse effects. Clinicians also noted that some patients may benefit from switching the PDE-5i to riociguat in combination with ERA.

- Clinicians advised that few newly diagnosed patients with PAH present with disease categorised as WHO FC I status, as these patients experience no symptoms during ordinary physical activity or at rest.
- Clinicians noted that application of the PBS restriction reference to WHO FC status can be subjective, and it is likely that patients may be classified by clinicians at a higher WHO FC (e.g. FC III rather than FC II to facilitate access to PBS subsidised dual therapy). Clinicians noted that, in some instances, the treatment unit or the patient themselves will fund the cost of the second agent (usually the less expensive PDE-5i), where ineligible for PBS-subsidised dual therapy. However, this is not always possible and highlights an inequity in access to optimal PAH treatment. Some clinicians further commented that it is counterintuitive to require patients with WHO FC II status to wait until their condition worsens before escalating to subsidised dual therapy.
- Clinicians noted that international clinical guidelines had been updated to support initiating dual drug therapy in newly diagnosed PAH patients with WHO FC II status and agreed that there is reasonable clinical evidence to support this practice.
- In general, treatment guidelines do not recommend monotherapy. Clinicians advised that patients prescribed initial monotherapy are likely those with an evolving diagnosis of pulmonary hypertension type, i.e. where a diagnosis of WHO Group 1 pulmonary hypertension (PAH) is not yet clear. Monotherapy may also be commenced in patients with PAH and cardiac risk factors, where escalation of treatment to dual therapy occurs more slowly and carefully than in patients without cardiac risk factors. The prevalence of cardiac risk factors (e.g. family history, systemic hypertension, diabetes, obesity and elevated cholesterol) and slightly elevated pulmonary capillary wedge pressure in the 12-15 mmHg range is high.
- Participants noted that 2022 ESC/ERS guidelines for pulmonary hypertension had lowered the mean pulmonary artery pressure (mPAP) threshold from at least 25 mmHg to greater than 20 mmHg, while PBS restrictions require that mPAP is at least 25 mmHg at rest. This represented a potential gap in PBS access for those patients with mPAP between 21 - 24 mmHg. Clinicians noted that clinical trial data and the 7th World Symposium in PH algorithm is based on patients with confirmed group 1 PAH based on mPAP of at least 25 mmHg with minimal data on therapy with a mPAP of 21-24 mmHg, hence changing the threshold in the PBS restriction would potentially be confusing. Most agreed that the number of patients with mPAP between 21-24 mmHg at diagnosis is likely to be very small and may not be offered therapy depending on risk assessment. Hence there is likely to be minimal financial impact to the PBS if the PBS restrictions were to remain silent on the threshold for PAH diagnosis.
- Clinicians agreed that a measure of response to treatment in the PBS restrictions for continuation of therapy was not necessary, stating that clinician judgement is assessing stability of disease and non-progression was adequate. Clinicians noted that patients who improved with PAH specific therapy rarely de-escalated oral therapy.

- Clinicians agreed that three-month intervals to assess response to dual therapy and the requirement to add on (and not up titrate) therapy was optimal.

The role of sotatercept in the PAH treatment paradigm

- Clinicians noted sotatercept's efficacy across a wide range of disease severity covering patients with functional class II symptoms (STELLAR trial), functional class II symptoms with intermediate or high risk of disease progression (HYPERION trial), functional class III symptoms (STELLAR, ZENITH trials), functional class III symptoms with intermediate to high risk of disease progression (HYPERION trial) and functional class IV symptoms (ZENITH trial).
- Participants noted that in March 2025, the PBAC considered and did not recommend a submission presenting evidence for use of sotatercept in patients with WHO FC II status and that, to date, a resubmission in this population or an application presenting clinical evidence for use in patients with more severe PAH had not been submitted for PBAC's consideration.
- Clinicians noted the benefits of using a disease modifying, anti-proliferative medicine early in the treatment paradigm, but agreed that in the context of limited Government budgets, PBS subsidy could initially be prioritised for the patient group likely to derive the most benefit – this patient group consists of patients at higher risk with WHO FC III-IV status with limited treatment options.
- Clinicians considered ERA plus a PDE-5i dual therapy would remain as the first-choice drug therapy in most patients. Sotatercept is associated with a high incidence of side-effects in clinical trials with very common side effects (experienced by 10 percent or more of trial subjects) ranging from rash, telangiectasia, erythema, diarrhea, increased haemoglobin, decreased platelets, antidrug antibodies, headache, dizziness and epistaxis. Common side effects (experienced by 1 to 10 percent of trial subjects) have been serious bleeding (e.g., gastrointestinal, intracranial haemorrhage) and severe thrombocytopenia (platelet count less than 50,000/mm3). Consequently, clinicians were doubtful that sotatercept would be used in patients with WHO functional class II status in place of an ERA plus PDE-5i.
- Clinicians suggested sotatercept therapy could be prioritised for patients in the following order:
  (1) Patients on maximum tolerated triple drug therapy that includes epoprostenol, 'as add on' therapy who would otherwise progress to either lung transplantation or death;
  (2) Patients who are receiving triple drug therapy that includes selexipag due to intolerance or inability to use epoprostenol;
  (3) Patients on dual drug therapy with inadequate response and where prostanoids are unsuitable (e.g., intravenous or inhaled prostacyclin is likely to pose practical difficulties in achieving compliance, selexipag associated diarrhoea in patients with scleroderma, inability to titrate selexipag doses via telehealth or to use epoprostenol due to rural/remoteness).
- Clinicians agreed that there is a large group of patients not adequately responding to dual therapy. One clinician estimated that using a validated risk calculator, approximately

20 percent of these patients would be considered to have a 'high risk' of mortality, and that a further 20 percent would be considered to have an 'intermediate to high risk' of mortality within the next 12 months. The clinician noted that these percentages may be underestimated due to the difficulty in gaining consent from various patient populations to be added to a PAH registry.

- Clinicians also estimated around 5 to 10 percent of patients are intolerant of prostanoids.
- Clinicians considered that initial uptake of sotatercept would be strong if PBS-listed because of the efficacy demonstrated in clinical trials to date and patient demand for a new treatment option, but that serious side effects are likely to be a deterrent to uptake of sotatercept in practice as well as a cause of patients discontinuing this therapy.
- Regarding the extent of replacement of PBS selexipag by sotatercept, clinicians noted that selexipag would be often worth trialling prior to considering sotatercept, despite the difficulties of dose titration and side effects, as a patient should have a high or intermediate-high risk assessment to justify the risk of sotatercept side effects versus benefits.
- Clinicians noted that while data on switching is currently limited, the flexibility to switch between selexipag, epoprostenol and sotatercept was needed to preserve patient choice of treatment options.
- Emerging treatments other than a potential oral form of sotatercept were not identified.

Conclusion

The PBAC Chair thanked participants for their time in attending the stakeholder meeting and the advice provided.