

# Consumer Outcome Statement

## Post-market Review of Pulmonary Arterial Hypertension Medicines

PHAA Members & Carers Day

Novotel Brighton Beach

Brighton Le Sands, New South Wales

14 October 2017

*This document is intended to provide a broad summary of the views expressed by patients with pulmonary arterial hypertension (PAH) and their carers gathered at the PHAA Members & Carers Day on 14 October 2017 or provided by members of the Pulmonary Hypertension Association Australia in writing by 31 October 2017. No attempt was made to reach consensus.*

### Abbreviations

6MWD	Six Minute Walk Distance
6MWT	Six Minute Walk Test
PAH	Pulmonary Arterial Hypertension
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PHAA	Pulmonary Hypertension Association Australia
PDE5	phosphodiesterase type 5
ToR	Terms of Reference
FC	Functional Class
WHO	World Health Organization

### Purpose and Context

The aim of the consumer session was to ensure that the final Report on the Post-market Review of PAH medicines (the Review) includes the views of a wide range of consumers and that these views inform the discussions about future options. The session was targeted at patients with PAH and their families and carers, all of whom are directly affected by access to medicines to treat this disease. The input from this session will help inform the Review's Report, which will be considered by the Pharmaceutical Benefits Advisory Committee (PBAC) and the Minister for Health in 2018.

The Review is being conducted under the Australian Government's Post-market Review Program for Pharmaceutical Benefits Scheme (PBS) medicines. An Expert Reference Group has been established to provide independent expert clinical advice and consumer input to the Review. A summary of the stakeholder input received at the consumer session will be included in the Review Report to the PBAC. The PBAC is an independent, expert committee that makes recommendations to the Government on the subsidy of medicines on the PBS.

Prior to the meeting, attendees were provided with a discussion paper that included information on the Review Terms of Reference (ToR), and identified key issues and questions for consumers and their families and carers. The questions from the discussion paper were used as the basis for prompting small group discussions at the consumer session.

Consumers and carers were also able to submit their responses to the discussion paper by email to [PBSsubmissionPMR@health.gov.au](mailto:PBSsubmissionPMR@health.gov.au) by 31 October 2017. Consumers were informed that the draft Review Report is expected to be publically available for comment prior to consideration by the PBAC sub-committees in the first half of 2018.

## Summary of Stakeholder Responses to Focus Questions

### ToR 1

*Review recent clinical guidelines for the management of PAH and compare this to the PBS restrictions and Therapeutic Goods Administration (TGA) indications for the use of PAH medicines.*

In February 2015, the Drug Utilisation Committee reviewed the PBS utilisation of PAH medicines, and noted that the PBS restrictions for PAH medicines are not consistent with the current European treatment guidelines in that they:

- Require patients with WHO functional class (FC) III to have failed to respond to six or more weeks appropriate treatment with a vasodilator (type of antihypertensive) when they have a mean right atrial pressure of 8 mmHg or less,
- Do not allow treatment of FC II patients, and
- Do not allow combination therapy.

### Identified Issue

There are differences between the international clinical guidelines for the treatment of PAH and the PBS restrictions for the use of PAH medicines.

### Question 1.1 What do you understand about PBS restrictions for PAH medicines?

- Consumers understood that they can currently access only one PAH medicine at any one time through the PBS. Consumers were also aware of the requirement to provide test results to support their ongoing treatment with PBS medicines.
- Consumers understood that patients in FC II are not eligible for PAH medicines under the PBS based on advice from medical practitioners. There was some confusion over continuing eligibility requirements, with some patients believing that the PBS PAH

medicines would no longer be available to them if/when the medicines led to an improvement in their health which saw them reclassified from FC III to FC II.

- Consumers noted that there are no specific medicines listed on the PBS for children and expressed a need for specific drugs and treatment regimens to be available for children.
- Consumers expressed frustration on the limited number of medicines available on the PBS (currently 8 medicines) in comparison to other countries such as Japan where they understood there to be up to 14 medicines available for PAH.
- Consumers considered it a priority to get access to:
  - multiple PBS-listed medicines at one time;
  - medicines for FC II to coincide with early diagnosis; and
  - a broad range of PAH medicines.
- Some consumers suggested that earlier treatment and combination therapy led to better health outcomes and questioned why treatment is not available for FC II patients whose health is only going to deteriorate. They also suggested that earlier treatment could be more cost-effective.

#### **Question 1.2 What do you know about international guidelines for the treatment of PAH?**

- Many consumers were unaware of the international guidelines for the treatment of PAH, but some understood that the guidelines provided information on the classification of PAH and treatments.

#### **ToR 2**

*Review the utilisation of PAH medicines in Australia, including sources of data that can provide additional information on clinical use that is not available from PBS data.*

The 2015 Drug Utilisation Committee report on the utilisation of PAH medicines through the PBS, provided the following key findings:

- The number of new patients starting on a PAH medicine is steady at approximately 420 patients each year.
- The total number of patients with PAH continues to increase over time, presumably due to improved survival. There were a total of 2026 patients receiving PBS subsidised PAH medicines in 2013.
- The age of patients initiating treatment has increased over the last decade. The mean age of new patients was 53.2 years in 2003/04 and was 64.1 years in 2013/14.

More recent PBS data (2016) show that the number of people treated continues to grow with approximately 2,400 patients now using PAH medicines

The PBS data is unable to provide information on PAH medicines that are obtained outside of the PBS. Therefore PBS data cannot inform the PBAC or government on all the medicines used by PAH patients in the community or in hospital.

## **Identified Issue**

Current PBS restrictions only allow the treatment of PAH patients with one PBS subsidised therapy at a time. Treatment is available for PAH patients in FC III and IV. In practice it is known that many patients are being treated with combination therapy and perhaps also receive treatment for FC II.

### **Q2.1 Are you currently using more than one PAH medicine in combination therapy? For what reason did you start a combination of PAH medicines? (i.e. your symptoms have recently worsened)**

- The majority of consumers advised that they were on dual or triple therapy.
- Some consumers started on dual/triple therapy at the time of diagnosis due to the severity of their disease.

### **Q2.2 Did you have difficulty accessing combination therapy?**

- Consumers voiced concerns about the confusion amongst some specialists on how to access medicines and noted varying degrees of knowledge amongst specialists across Australia. Consumers noted that a personal background in health helps to manoeuvre the system.
- Others found that the medical specialist and hospitals arranged access to combination therapy, including through drug trials.

### **Q2.3 How do you access the non-PBS funded medicines? Do you obtain your medicines through compassionate access programs, through hospitals or buy them privately?**

- Consumers access medicines through a range (and combination) of avenues, including through the PBS, hospitals, drug trials, and compassionate access programs or private funding (often sildenafil).
- Some consumers were not sure where medicines come from or how they are subsidised, while others were well informed.

### **Q2.4 What are the impacts on you and your family of accessing supplementary medicines outside the PBS?**

- Consumers experience anxiety about the continued availability of PAH medicines, especially at the time when particular pharmaceutical access programs or drug trials end.
- Consumers noted the financial burden for themselves, family and friends. This included the cost of PBS co-payments for medicines (non-concessional), cost of privately funded medicines and accessories, such needles and syringes, dressings of permanent IV lines, oxygen and/or other tests.
- The financial burden impacts particularly on families with dependent children, who experience reduced income (from patients unable to work) paired with higher medical expenses.
- Several patients who had dependent children stated “access was stressful but that they had no option, because they needed the medicines to be able to care for their children every day”.

- Lengthy travel times and the need for overnight stays to attend regular hospital appointments impact on some consumers and their families to access medicines through drug trials.

### **Q2.5 Did you access PAH medicines for FC II PAH?**

- Consumers discussed that PBS-listed medicines should be available for FC II PAH.
- Some consumers received PAH medicines for FC II, while others were diagnosed at FC III or IV.
- Some consumers reported that they were not able to be prescribed medicines once they improved from FC III or IV and were reclassified as FC II.

### **ToR 3**

*Review the clinical outcomes that are most important or clinically relevant to patients with PAH, and the extent to which these outcomes are included in the evidence previously considered by PBAC.*

Clinical trials are undertaken by pharmaceutical companies to assess if and how well medicines work and how safe they are. These studies may also show which medicines work best for certain illnesses or groups of people. Historically, the PBAC has considered the studies that measure Six Minute Walk Distance (6MWD) as the main outcome when assessing PAH medicines.

Clinical trials for PAH medicines measure a range of other clinical outcomes such as changes in WHO FC, arterial blood pressure, adverse events such as hospitalisation, and survival.

Treatment goals have evolved over time to become more patient centred and can include attaining FC II status, an improved 6MWD and haemodynamic test improvements.

The most commonly reported symptoms of PAH from patients are fatigue, chest pain, syncope (fainting), difficulty breathing and reduced ability to perform daily physical activities – all of which have an extensive impact on patients' quality of life.

### **Identified Issue**

There is concern that the outcomes measured in clinical trials and considered by the PBAC may not represent what is most clinically important to patients.

### **Q3.1 How have PAH medicines made a difference to your symptoms and daily life?**

- Consumers noted that medicines made a significant difference to their lives.
- Consumers noted specific relief of PAH symptoms with ongoing medicine use, noting less fatigue, breathlessness and heart racing. Consumers valued that they feel more 'normal' and can function in everyday life when taking PAH medicines.
- Some consumers reported they had improved from the point of heart failure to FC II, where they were able to come off the transplant list and recommence a semi normal life.

### **Q3.2 What changes in your health do you value the most?**

- Consumers valued the ability to function in everyday life and the increased tolerance to exercise. Everyday activities described included the ability to work, get out of bed, attend to household chores, be able to socialise, to climb stairs and walk further.
- Some consumers valued that they were able to travel and compete in sporting events.
- Consumers noted that the PAH medicines resulted in an improvement in their quality of life. Some consumers wished they were well enough to continue working.
- Others valued that they were alive, were able to breathe and no longer required a lung transplant.
- Consumers noted reduced anxiety when their PAH was stable.

### **Q3.3 Are important changes in your health reflected in clinical measures such as the 6MWD or rates of hospitalisation?**

- Consumers commented that the 6MWD can be somewhat subjective, as the results are a 'snapshot' of their overall health only. They noted that results can change daily and can be impacted by travel on the day of the test, the test area or prior stair climbing.
- Consumers tended to plan for the 6 Minute Walk Test (6MWT).
- Consumers did relate improvements in the 6MWD to the effectiveness of PAH medicines.
- Consumers considered the Right Heart Catheterisation is invasive but more accurate than the 6MWT for some.
- Some consumers described their health status by referring to their FC and/or 6MWD, while others considered that their condition fluctuates and therefore the WHO FC status is changeable.

### **Q3.4 Are there side effects from PAH medicines that impact negatively on your daily activities and quality of life?**

- Consumers generally considered that the benefits gained from PAH medicines outweighed the side effects. Many consumers described side effects ranging from minor to severe, including headaches, sinus, jaw and muscle pain, foot pain, dizziness, chest tightness, gastro complications, palpitations and flushing.
- Consumers also noted the issues associated with IV lines, such as infections and allergic reactions to the dressings.
- Consumers used medicines to treat the side effects, such as pain killers.
- Consumers discussed sildenafil, some of which is sourced privately. They noted that the dosage they used could be variable when (unscored) tablets are split (some consumers found generic brands of tablets also crumbled more easily). Different brands of sildenafil can also cause/exacerbate side effects, such as diarrhoea and headaches. Sildenafil (and to a lesser extent, tadalafil) can cause unwanted erections in males.
- Consumers mentioned that sometimes instructions on prescriptions for sildenafil were incorrect, and advised patients to take it three times daily, instead of every eight hours.

**Q3.5 Are there any other clinical outcomes that should be highlighted to the PBAC when they consider the effectiveness of PAH medicines?**

- Consumers did not note any other clinical outcomes for consideration by PBAC.
- Written submissions noted the following outcomes were patient relevant and may also be used to inform considerations of the effectiveness of PAH medicines:
  - Right heart catheter measurements
  - Echocardiogram outcomes
  - Changes in oxygen use from medications
  - Everyday functional ability
  - Changes in exercise capacity
  - Ability to work part-time/full-time
  - Walking distance in social situation
  - Ability to travel

**ToR 4**

*Collate and evaluate evidence on the comparative effectiveness of PAH medicines, including combination use and use in the WHO functional class II patient populations.*

**Identified Issue**

Changes to the PBS restrictions to allow combination therapy and/or treatment of FC II patients will require evidence to support the use of PAH medicines in these populations and combinations.

**Q4.1 Which combination therapies are you using?**

- Consumers on combination therapy tended to be using various double and triple combinations of endothelin receptor antagonists with phosphodiesterase type 5 inhibitor (PDE5) inhibitors and prostacyclins.
- Some consumers participated in drug trials, including for bardoxolone methyl (Catalyst trial) and oral trepostinil, a prostacyclin analogue.
- There were reports of patients in the PHAA using selexipag also.

**Q4.2 Do the PAH medicines you use continue to be effective? Have you swapped medicines or added additional medicines?**

- Consumers advised that they usually stay on the same medicines and add a further medicine to address worsening symptoms.
- Consumers swapped medicines to alleviate side-effects or because they proved ineffective.

**Q4.3 Do you find some PAH medicines better than others, in regards to symptom relief, side effects and how you take it (tablet, inhalation, infusion)?**

- Consumers mentioned that some drugs worked better than others.
- Consumers pointed out that continuous intravenous administration of epoprostenol, while effective, leads to considerable inconvenience and additional cost for accessories and dressings. In addition there is a risk of catheter-related infection. Some consumers

reported preferring the nebulised prostacyclins which although had more frequent dosing, were less invasive.

- Epoprostenol users generally have a backup infusion pump and intravenous infusion sets.
- Consumers noted it is easier to take tablets twice daily than tablets three times daily.

**Q4.4 Are there any PAH medicines you have used which did not relieve your symptoms?**

- Consumers identified some PAH medicines which did not work in their particular case. (macitentan x2, sildenafil, iloprost, beraprost).

**Q4.5 Have you taken PAH medicines which have impacted other medicines you take?**

- Generally consumers found that PAH medicines did not impact on other medicines.
- Some advised they could not take cold/flu medicines or antihistamines or anti-inflammatory medicines.

**Other**

- Consumers noted that access to a continuing and reliable supply of PAH medicines could be problematic in rural areas as local pharmacies usually do not carry stock. The supply can be disrupted and cause shortages, such as when flooding and road closures occur.
- Consumers noted the difficulties associated with travelling to hospital to pick up medicines, including lengthy travel time and the need to stay overnight. Some noted that home delivery was being introduced.
- Consumers noted a lack of research relevant to children with PAH.