

# Semaglutide Stakeholder Meeting Outcome Statement

Thursday 26 August 2021

## Attendees

Members of the Pharmaceutical Benefits Advisory Committee (PBAC), clinicians with expertise in the management of overweight and obesity, including a Staff Specialist in Endocrinology, Royal North Shore Hospital, representatives from the Obesity Collective, consumer groups, Novo Nordisk Pharmaceuticals, and the Department of Health were in attendance.

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

## Purpose of meeting

The PBAC Chair outlined that the objective of the stakeholder meeting was to discuss:

- The burden of disease of overweight and obesity, and the nature of these conditions.
- The population suitable for pharmacotherapy/semaglutide.
- Which clinical measure should be used in criteria (e.g. BMI, or other) – what is clinically meaningful, well known to prescribers and easy to implement?
- What should be the clinical criteria for PBS Initiation and Continuation?
- Which prescribers types should be eligible to prescribe PBS semaglutide? Should there be different prescribing authority for PBS Initiation versus Continuation?
- What other therapy should precede pharmacotherapy (diet, exercise, behavioural therapy etc), and how should a reasonable trial of these prior to progressing to drug treatment be defined?
- What is the goal of treatment? Quality of life gains from weight loss or improved long-term health outcomes / reduction in comorbidities, or both?

The discussion was expected to be around pharmacotherapy generally, as well as semaglutide specifically.

## Background

Overweight and obesity has a high public health burden in Australia, affecting an estimated 2 in 3 Australians aged 18 and over, or around 12.5 million adults. In 2015, 8.4% of the total disease burden in Australia was due to overweight and obesity, and it is the leading risk factor contributing to non-fatal disease burden. Having overweight or living with obesity increases a person's likelihood of developing many chronic conditions, such as cardiovascular disease, diabetes, asthma, back problems, chronic kidney disease, dementia, and some cancers. In addition, when examining all causes of death, it is associated with a higher death rate (Australian Institute of Health and Welfare, [Australia's health 2020](#)), as is being below a healthy weight range.

There are currently no therapies for overweight or obesity on the Pharmaceutical Benefits Scheme (PBS).<sup>1</sup> Semaglutide for weight management was accepted for evaluation by the Therapeutic Goods Administration in March 2021, and an application for PBS listing is expected. The PBAC convened a stakeholder meeting due to the high public health burden, and to help inform its future consideration of issues relating to the proposed PBS population and health outcomes to be valued.

Semaglutide is a glucagon-like peptide-1 receptor agonist and is currently available on the PBS as an Authority Required (Streamlined) benefit for type 2 diabetes, for which it is administered as a once weekly injection in doses of up to 1 mg per week. Semaglutide for weight management is expected to be delivered as a weekly 2.4 mg injection. The sponsor's trial program includes the Semaglutide Treatment Effect in People with obesity (STEP) program (including STEP 1-8) and the Semaglutide Effects on Heart Disease and Stroke in Patients With Overweight or Obesity (SELECT) trial.

## Discussion and outcomes

### Burden of disease of and population suitable for pharmacotherapy

- Stakeholders noted the large number of people affected by overweight and obesity in Australia, and the broad population eligible for semaglutide in the STEP program. The PBAC Chair explained that it was likely that the sponsor, and the PBAC, will need to define a PBS population of patients who will see the most benefit, sustain that benefit, and adhere to treatment (in order to be cost-effective at the price proposed by the sponsor).
- Stakeholders discussed the significant heterogeneity<sup>2</sup> of obesity and how it is essential that a person-centred approach to treatment is available. This would involve a thorough intake assessment that would cover the possibility of eating disorders, mental health conditions, experience of trauma (including childhood trauma), metabolic and/or hormonal conditions, other physical conditions, as well as what the patient knows about what has worked well for them in the past, and what their current situation is regarding other social determinants of health.
- Stakeholders also discussed the range of measures available to health care professionals in managing overweight and obesity, including lifestyle interventions (defined as healthy nutrition, exercise +/- behavioural therapies) either alone, or in conjunction with pharmacotherapy or bariatric surgery (which is a step-wise approach in chronic disease management). It was commented that semaglutide would be a useful addition to the therapeutic armamentarium.
- It was observed there are populations in different settings that may be suitable for pharmacotherapy:
  - In general practice, and other specialist or hospital-based weight loss and metabolic clinics, patients typically arrive having not responded to several attempts at weight loss, noting that not all of these will have been health interventions as many people try a range of commercial weight loss

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<sup>1</sup> Orlistat is available as an Authority Required benefit for obesity on the Repatriation Pharmaceutical Benefits Scheme only.

<sup>2</sup> Ian J. Neeland, Paul Poirier, and Jean-Pierre Després, "Cardiovascular and Metabolic Heterogeneity of Obesity: Clinical Challenges and Implications for Management", *Circulation* 137, no. 13 (2018): 1391–1406, <https://doi.org/10.1161/CIRCULATIONAHA.117.029617>.

approaches, and they are wanting to lose weight and maintain weight loss in the longer term.

- In hospital and other specialist settings, patients can also require short term weight loss in order to be eligible for transplant or other surgery (it was noted that State/Territory funding to support weight loss in such circumstances may be available for these patients via alternative means.)
- Stakeholders agreed that there were substantial barriers to accessing bariatric surgery, which is well documented as the most effective anti-obesity therapy which is currently available. The issue of inequity was raised given that bariatric surgery is primarily delivered in private hospitals, with less than 10%<sup>3</sup> being delivered in public hospitals due to long waiting times for public services, limited staff and resources and lack of/insufficient provision of public services in regional and remote areas, where there is high need. Stakeholders did not consider that bariatric surgery would be the therapy most likely to be replaced in practice by semaglutide (although some noted the rapidly growing proportion of Australians with severe obesity who would be potentially eligible for bariatric surgery). Rather, it was expected to be used largely as an add-on therapy to other lifestyle interventions as outlined above.
- Some comments suggested that highest clinical need would be in patients who are at the more severe end of the overweight/obesity spectrum, while other comments suggested that pharmacological treatment should take place earlier in the disease course before weight-related complications arise. Reference to Padwal et al<sup>4</sup> looking at the United States National Health and Human Nutrition Examination Surveys and Edmonton obesity staging system data was discussed during the meeting, as a source that identifies which groups of patients are likely to benefit the most from anti-obesity therapy from a morbidity and mortality perspective.
- It was noted that patients treated in Australian clinical practice may be less healthy and certainly less supported than those receiving therapy in the structured and controlled environment of the sponsor's trial program. For example, patients in the Australian population may have additional comorbidities, which were excluded in the trial.
- Stakeholders considered that there were different goals of treatment in different populations/clinical settings.

### Goals of pharmacological treatment

- As noted above, for some patients, the goal of pharmacological therapy would be to achieve short term weight loss (e.g. pre-transplant), but for the majority, the goal would be to achieve sustained weight loss, in order to reduce the likelihood of developing a range of comorbidities, such as micro/macrovascular disease complications from type 2 diabetes, cardiovascular disease, prevention of progression from pre-diabetes to diabetes, sleep apnoea and chronic kidney disease.

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<sup>3</sup> Backman B, Brown D, Cottrell J, Campbell A, Clancy W, Halim Shah Y J, Chadwick C, Budin A, MacCormick A, Caterson I and Brown W. The Bariatric Surgery Registry Annual Report, 2020. Monash University, Department of Epidemiology and Preventive Medicine. August 2020, Report No. 8

<sup>4</sup> Raj S. Padwal, Nicholas M. Pajewski, David B. Allison and Arya M. Sharma, "Using the Edmonton obesity staging system to predict mortality in a population-representative cohort of people with overweight and obesity", *Canadian Medical Association Journal* 183, no. 14 (October 2011): E1059-E1066, <https://doi.org/10.1503/cmaj.110387>.

- From a patient perspective, other important goals include improved quality of life, particularly with respect to mental wellbeing since the psychological burden of repeated non-response to weight loss interventions can become very challenging over time. It was commented that it could be further damaging to some patients if pharmacotherapy became ‘yet another tried and failed’ attempt at weight loss, which was a segue to the issue of stigma and shame many people with overweight/obesity experience. It was suggested, as per the World Obesity Federation recommendations, that terminology is important, for example, the use of “responder” vs “non responder” to therapy should be adopted instead of “success” vs “fail” therapy.
- Stakeholders agreed that it was therefore important to target treatment towards patients who would be most likely to achieve sustained weight loss. In terms of quality of life, some concerns were also raised with respect to the burden of weekly semaglutide injections and the experience of gastrointestinal adverse events (AEs) in the key clinical trials. However, the clinical viewpoint was that a weekly injection is tolerated for many medicines such as insulin, some other hypoglycemic agents, migraine therapy and anticoagulants, and should not be a substantial deterrent to uptake and adherence to treatment. However, there was no discussion about the potential impact of gastrointestinal AEs on the long-term compliance with the medication regime.
- Some stakeholders raised the importance of nutritional guidance, alongside use of semaglutide, to attain optimal health outcomes.
- There was also some discussion around the degree of sustained weight loss required to achieve a reduction in the risk of developing long term complications, which was generally considered to be around 10%.
- Patients with very high BMI (e.g. 50 kg/m<sup>2</sup> or greater), or older patients with overweight and obesity may already have established complications and comorbidities, and thus it was suggested that the goal of treatment might also be to see an amelioration in comorbidities or slowing of deterioration (moreover, some stakeholders considered that the weight loss required to see risk reductions in patients with a very high BMI may be greater than 15%).
- Stakeholders noted that no trial data for long-term benefits for weight loss are currently available, although ongoing studies to address this are underway. Therefore, the sponsor commented that some extrapolation of benefits will be required in the economic evaluation for semaglutide.

#### Potential initiation and continuation criteria

- Stakeholders also discussed the PBS initiation and continuation criteria (to reflect the population suitable for therapy and the expected health outcomes to be purchased).
- Some clinician stakeholders, particularly in general practice and endocrinology, expressed that they would like the option for GPs to offer and prescribe semaglutide to suitable patients where clinically indicated, given that primary care is often the first point of contact with the Australian healthcare system. GPs have extensive and well published experience in chronic disease management and often have the infrastructure in place to offer the multidisciplinary care required for the long-term management of a chronic disease. They considered that the key clinical trials would provide a strong evidence base for informing PBS eligibility.
- Specifically, it was noted that participants in the STEP trials had a mean BMI of over 35 kg/m<sup>2</sup> or more, and between 44%-90% of participants had two or more co-morbidities

across the trials, including, hypertension, coronary artery disease, pre-diabetes, hyperlipidaemia, asthma. It was also noted that close to 50% of participants had pre-diabetes.

- In terms of continuation with therapy, stakeholders agreed that patients should be assessed for response in order to continue treatment. Response was variously suggested to include a percentage weight loss, improved quality of life, and possibly in some cases, an improvement in comorbidities. However, it was noted that the dosing regimen required a period of titration, and patients would need 12-14 weeks at a stable dose, so assessment for continuation should not be conducted earlier than 20 weeks.
- The PBAC Chair queried whether semaglutide would potentially be a lifelong treatment. Some stakeholders considered that if a patient achieved weight loss, and then ceased therapy, they would likely put weight back on due to metabolic adaptation. Therefore, it may be appropriate for patients to continue with treatment if responding, and only cease therapy if no response achieved or weight loss not maintained.
- Stakeholders considered that many patients present for treatment in general practice following multiple prior attempts at weight loss. Some stakeholders considered it unlikely that results from previous attempts would be a good indicator of future results, and it was suggested that concurrently co-prescribing semaglutide with healthy lifestyle changes would be essential.

#### Prescriber types

- Stakeholders noted that equity of access to specialised overweight and obesity care is currently an issue in Australia both in terms of waiting times for bariatric services and metabolic clinics, and distance to services for rural and remote communities (although some telehealth services currently exist).
- Stakeholders were generally in agreement that restricting semaglutide prescribing to specialist services would result in similar issues of inequity of access and prolonged waiting periods resulting in worsening of obesity and its associated health sequelae, and that positioning the therapy only in specialist settings would not allow it to reach all patients expected to benefit from treatment. However, the benefit of consumers being able to receive weight management care from people with specialist training in the area was highlighted by the consumer stakeholder. Many consumers may experience sub-optimal care in the format of incomplete or out of date advice from generalist clinicians. It may be appropriate for prescribers to undertake regular contemporary training specifically in the area of weight management.
- Some stakeholders noted that weight management services include nurse-led care models with holistic, multi-faceted approaches, and regular contact (e.g. fortnightly). From a clinical perspective, it was noted that patients achieve optimal outcomes when they have an ongoing relationship with a health care professional. From a patient perspective, it was noted that patients value a continuing connection with a single health care provider who is adequately trained in weight management.
- The discussion considered it may be appropriate to restrict semaglutide prescribing to those (in general practice or otherwise) with particular qualifications or certifications in weight management (e.g. SCOPE certification from the World Obesity Federation). Concern was raised that this may cause issues for equitable access.

## **Conclusion**

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

The sponsor indicated its intention to use the advice provided to inform a future submission for listing semaglutide on the PBS.