

7.14 SEMAGLUTIDE

**Injection, 2.0 mg in 1.5 mL and 4.0 mg in 3.0 mL pre-filled syringe,
Ozempic[®],
Novo Nordisk Pharmaceuticals Pty Ltd**

1 Purpose of Application

- 1.1 The minor submission requested an amendment to the November 2019 PBAC advice regarding the therapeutic relativity such that both semaglutide 0.5 mg and 1.0 mg are considered equi-effective to dulaglutide 1.5 mg for use in combination with metformin and/or a sulfonylurea for the treatment of patients with Type 2 Diabetes Mellitus (T2DM).
- 1.2 The minor submission also requested flat pricing for the two semaglutide dosage forms.

2 Background

Registration status

- 2.1 Semaglutide (injectable) was TGA registered on 28 August 2019 for treatment of adults with insufficiently controlled T2DM as an adjunct to diet and exercise:
- As monotherapy when metformin is not tolerated or contraindicated
 - In addition to other medicinal products for the treatment of T2DM.

Previous PBAC consideration

- 2.2 Semaglutide was previously recommended for this form and indication by the PBAC at its November 2019 meeting.
- 2.3 A summary of the previous submission and current submission is provided in the table below.

Table 1: Summary of the previous submission and current resubmission

	November 2019 submission	Current resubmission
Requested PBS listing	The submission requested a Section 85, Authority Required (STREAMLINED) listing for semaglutide (injectable) for treatment of patients with T2DM who have inadequate glycaemic control, as dual therapy in combination with metformin or a sulfonylurea where either of these is contraindicated or not tolerated; or triple therapy in combination with metformin and a sulfonylurea. (para 1.1)	The proposed PBS listing is the same as requested in the November 2019 major submission. In the event that the PBAC does not amend its advice on the therapeutic relativity and equi-effective doses of semaglutide and dulaglutide, the Sponsor proposed an alternative listing scenario entailing initial and continuing treatment phases which would restrict use of the 1.5 mL pen device to initial therapy only.
Requested effective DPMQs	\$ [REDACTED] (para 6.93)	\$ [REDACTED]

Public Summary Document – March 2020 PBAC Meeting

	November 2019 submission	Current resubmission
Comparator	<p>The submission nominated exenatide once weekly as the main comparator and dulaglutide once weekly as the secondary comparator. (para 5.1 & 5.2)</p> <p>The PBAC considered that both exenatide and dulaglutide should be considered comparators. (para 7.4)</p>	<p>The submission nominated dulaglutide 1.5 mg once weekly as the comparator.</p>
Clinical evidence	<p>Direct comparison of</p> <ul style="list-style-type: none"> • semaglutide 1.0 mg once weekly and exenatide 2.0 mg once weekly; and • semaglutide 0.5 mg once weekly with dulaglutide 0.75 mg once weekly; • semaglutide 1.0 mg once weekly with dulaglutide 1.5 mg once weekly. <p>The Pre-Sub-Committee Response (PSCR) provided results from a post-hoc cross dose analysis comparing 0.5 mg semaglutide once weekly and 1.5 mg dulaglutide once weekly.</p> <p>Supportive cardiovascular safety and long-term outcomes data of semaglutide 0.5 mg once weekly and semaglutide 1.0 mg once weekly versus placebo.</p>	<p>Unchanged</p>
Key effectiveness data	<p>Primary outcome of change in HbA1c and secondary outcome of change in bodyweight.</p>	<p>The submission presented additional details from the SUSTAIN 7 trial, including the post-hoc analysis of this comparison, as presented in the PSCR in November 2019.</p>

Public Summary Document – March 2020 PBAC Meeting

	November 2019 submission	Current resubmission
Clinical claim	<p>Claim of superiority in terms of effectiveness and non-inferiority in terms of safety for semaglutide 1.0 mg compared to exenatide 2.0 mg once weekly when used as dual or triple therapy with metformin and/or sulfonylurea. (para 6.60)</p> <p>No claim was made for semaglutide 0.5 mg versus exenatide 2.0 mg. (para 6.61)</p> <p>Claim of superiority in terms of efficacy and non-inferiority in terms of safety for semaglutide (0.5mg or 1mg weekly) compared with dulaglutide 1.5 mg once weekly in dual therapy with metformin or sulfonylurea. (para 6.62, 6.63)</p> <p>No claim was made for semaglutide (0.5 mg or 1.0 mg) once weekly versus dulaglutide 1.5 mg once weekly in triple therapy with metformin and sulfonylurea. (para 6.64)</p> <p>The PBAC previously accepted semaglutide as non-inferior in terms of effectiveness to dulaglutide (para 7.10) and a claim of non-inferior safety for semaglutide 1.0 mg and dulaglutide 1.5 mg (para 7.9).</p> <p>The PBAC recommended 1.0 mg semaglutide once weekly was equi-effective to 1.5 mg dulaglutide once weekly (para 7.14).</p>	<p>Semaglutide (both 0.5 mg and 1 mg weekly regimens) is at least non-inferior in terms of efficacy and similar in terms of safety to dulaglutide 1.5mg once weekly when used as dual or triple therapy with metformin and/or a sulfonylurea.</p>
Economic evaluation	<p>The submission proposed a cost-utility analysis compared to exenatide once weekly.</p> <p>The PBAC considered that the cost-effectiveness of semaglutide would be appropriate if it were cost-minimised to dulaglutide. (para 7.2)</p>	<p>The resubmission presented a cost minimisation analysis of semaglutide (either 0.5 mg or 1 mg weekly) and dulaglutide 1.5 mg weekly.</p>
Number of prescriptions	<p>Estimated 50,000 – 100,000 in year 1, increasing to over 200,000 in year 6.</p> <p>The submission assumed semaglutide would substitute for exenatide, dulaglutide, sitagliptin (proxy for DPP4) and empagliflozin (proxy for SGLT2 inhibitors). The submission also assumed some substitution for insulin glargine in years 4-6.</p>	<p>Estimate 50,000 – 100,000 prescriptions in year 1, increasing to 100,000 – 200,000 in year 6.</p> <p>The resubmission assumed simple substitution of semaglutide for dulaglutide on a 1:1 basis.</p>
Estimated net cost to PBS	<p>Less than \$10 million cost in year 1 increasing to \$30 - \$60 million cost in year 6.</p>	<p>The resubmission assumed that listing of semaglutide would be cost neutral as it will replace use of dulaglutide and/or exenatide which have the same or higher price, respectively.</p>
Risk sharing arrangement	<p>Not requested</p>	<p>Not requested</p>

	November 2019 submission	Current resubmission
PBAC decision	Recommend PBAC Comment: The PBAC recommended the listing of semaglutide (injectable) for treatment of patients with T2DM who have inadequate glycaemic control, as dual therapy in combination with metformin or a sulfonylurea where either of these is contraindicated or not tolerated; or triple therapy in combination with metformin and a sulfonylurea. (para 7.1)	-

Source: Compiled during the evaluation. Paragraph references for November 2019 refer to the semaglutide PBAC Public Summary Document.

For more detail on PBAC’s view, see section 6 PBAC outcome.

3 Requested listing

- 3.1 The proposed preferred PBS listing was the same as that recommended by the PBAC in November 2019. (See para 8.1, semaglutide Public Summary Document (PSD), November 2019 PBAC meeting)
- 3.2 The submission also proposed an alternative listing in the event that the PBAC did not amend its advice on the therapeutic relativity and equi-effective doses of semaglutide and dulaglutide (see below). The key differences between the proposed alternative PBS listing and the previously recommended restriction are:
 - Two initial treatment phase listings (dual and triple therapy) for the semaglutide 2 mg / 1.5 mL presentation to allow titration of treatment. Only 1 repeat was proposed for these initial treatment phase listings, compared to 5 repeats in the previously recommended restriction for both presentations.
 - A continuing treatment phase listing for the semaglutide 4 mg / 3.0 mL presentation only.
- 3.3 The PBAC noted that the 4.0 mg / 3 mL pen does not allow for the delivery of the 0.5 mg dose and therefore restricting prescribing of the 2 mg / 1.5 mL pen to commencement therapy would prevent patients from being maintained on the 0.5 mg dose and this would not be clinically appropriate (semaglutide approved Product Information).

For more detail on PBAC’s view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The minor submission identified dulaglutide as the appropriate comparator.
- 4.2 In November 2019, the PBAC advised that both exenatide and dulaglutide should be considered comparators to semaglutide (paragraph 7.4, semaglutide PSD, November 2019 PBAC meeting). The PBAC’s recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of semaglutide would be

acceptable if it were cost-minimised against dulaglutide (paragraph 7.2, semaglutide PSD, November 2019 PBAC meeting).

For more detail on PBAC’s view, see section 6 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

5.3 As a minor submission, no new clinical trials were presented in the submission. The data presented was based on the clinical trials presented in the November 2019 submission.

5.4 Details of the trials presented in the November 2019 submission are provided in the table below.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
SUSTAIN 3 (NCT01885208)	Novo Nordisk Clinical Trial Report (2016). Efficacy and safety of semaglutide once-weekly versus exenatide ER 2.0 mg once-weekly as add-on to 1-2 oral antidiabetic drugs (OADs) in subjects with type 2 diabetes	Internal study report
	Ahmann AJ, Capehorn M, Charpentier G et al (2018). Efficacy and Safety of Once-Weekly Semaglutide Versus Exenatide ER in Subjects With Type 2 Diabetes (SUSTAIN 3): A 56-Week, Open-Label, Randomized Clinical Trial	Diabetes Care;41(2):258-266
SUSTAIN 7 (NCT02648204)	Novo Nordisk Clinical Trial Report (2017). Efficacy and safety of semaglutide versus dulaglutide as add-on to metformin in subjects with type 2 diabetes	Internal study report
	Pratley RE, Aroda VR, Lingvay I et al (2018). Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial	Lancet Diabetes & Endocrinology;6(4):275-86
SUSTAIN 6 (NCT01720446)	Novo Nordisk Clinical Trial Report (2016). A long-term, randomised, double-blind, placebo-controlled, multinational, multi-centre trial to evaluate cardiovascular and other long-term outcomes with semaglutide in subjects with type 2 diabetes	Internal study report
	Marso SP, Bain SC, Consoli A et al (2016). Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes	New England Journal of Medicine;375(19):1834-1844

Source: Table 2, semaglutide Public Summary Document, November 2019 PBAC meeting

5.5 Additional details of the SUSTAIN 7 trial to address the issue of the relativity of the semaglutide 0.5 mg dose with dulaglutide 1.5 mg dose were presented, including the post-hoc analysis of this comparison, as presented in the Pre-Sub-Committee Response in November 2019.

Comparative effectiveness

- 5.6 The resubmission presented data from the pre-specified high dose and post-hoc cross dose comparisons of dulaglutide 1.5 mg versus semaglutide 1.0 mg and semaglutide 0.5 mg respectively (Table 3).

Table 3: Summary of results of the post hoc analyses of SUSTAIN 7

Outcome	SEM 0.5 mg	SEM 1.0 mg	DUL 1.5 mg	SEM 0.5 vs. DUL 1.5	SEM 1.0 vs. DUL 1.5
Inferential non-inferiority analyses (mean change from baseline)				Mean difference [95% CI]	
HbA1c (%)	-1.51	-1.78	-1.37	-0.14 [-0.30; 0.01]	-0.41 [-0.57; -0.25]
Body weight (kg)	-4.56	-6.53	-2.98	-1.58 [-2.35; -0.82]	-3.55 [-4.32; -2.78]
Body weight (%)	-4.92	-6.92	-3.26	-1.66 [-2.46; -0.86]	-3.67 [-4.47; -2.86]
Inferential sensitivity analyses (HbA1c)				Mean difference [95% CI]	
Per-protocol	-1.53	-1.78	-1.40	-0.13 [-0.29; 0.02]	-0.38 [-0.54; -0.22]
Complete cases	-1.52	-1.82	-1.41	-0.11 [-0.26; 0.05]	-0.41 [-0.57; -0.26]
LOCF	-1.41	-1.64	-1.32	-0.09 [-0.24; 0.06]	-0.32 [-0.47; -0.17]
Retrieved dropout	-1.40	-1.62	-1.29	-0.12 [-0.30; 0.07]	-0.34 [-0.52; -0.15]
Inferential sensitivity analyses (body weight in kg)				Mean difference [95% CI]	
LOCF	-4.25	-5.97	-1.94	-1.31 [-2.01; -0.61]*	-3.03 [-3.73; -2.32]
Retrieved dropout	-4.18	-5.85	-2.80	-1.39 [-2.19; -0.59]*	-3.05 [-3.85; -2.25]
Patients achieving clinically important outcomes (odds)				Odds Ratio [95% CI]	
HbA1c < 7.0%	2.54	4.26	2.18	1.17 [0.78; 1.73]	1.96 [1.28; 3.00]
Weight loss > 5%	0.77	1.46	0.48	1.60 [1.12; 2.29]	3.03 [2.11; 4.34]
Composite outcome	1.91	2.87	1.33	1.44 [0.98; 2.09]	2.15 [1.45; 3.19]
Supportive clinical/laboratory outcomes (change from baseline)				Mean difference [95% CI]	
FPG (mmol/L)	-7.53	-6.88	-7.46	0.07 [-0.26; 0.39]	-0.58 [-0.91; -0.26]
HDL ratio (mmol/L)	0.99	1.01	1.02	0.97 [0.95; 0.99]	1.00 [0.98; 1.02]
LDL ratio (mmol/L)	0.97	1.00	1.01	0.96 [0.92; 1.00]	0.99 [0.95; 1.04]
TC ratio (mmol/L)	0.96	0.97	0.99	0.97 [0.95; 1.00]	0.98 [0.96; 1.01]
TG (mmol/L)	0.91	0.86	0.90	1.02 [0.96; 1.08]	0.96 [0.91; 1.02]
BMI (mg/kg ²)	-1.63	-2.33	-1.08	-0.55 [-0.82; -0.28]	-1.25 [-1.52; -0.98]
DBP (mmHg)	-0.57	-2.05	-0.03	-0.54 [-1.86; 0.79]	-2.0 [-3.4; -0.7]
SBP (mmHg)	-2.44	-4.88	-2.86	0.42 [-1.68; 2.52]	-2.0 [-4.1; 0.1]
Health Related Quality of Life (change from baseline)				Mean difference [95% CI]	
SF-36 (PCS)	1.21	2.04	1.29	-0.08 [-1.18; 1.01]	0.75 [-0.35; 1.85]
SF-36 (MCS)	1.45	1.23	1.08	0.37 [-0.98; 1.71]	0.15 [-1.20; 1.50]
DTSQ (TS)	4.60	4.55	4.65	-0.05 [-0.83; 0.74]	-0.10 [-0.89; 0.70]

Source: Table 3, pg 7 of the resubmission

- 5.7 The difference in HbA1c reduction between semaglutide 0.5 mg and dulaglutide 1.5 mg was not statistically significant, with the point estimate favouring semaglutide (-0.14, 95% CI (-0.30; 0.01)). More patients achieved an HbA1c of <7.0% with semaglutide 0.5 mg than dulaglutide, although this outcome was not statistically significant. The ESC previously considered that the treatment difference in HbA1c reduction between semaglutide 1.0 mg and dulaglutide was not clinically significant. (para 6.24, semaglutide PSD, November 2019 PBAC meeting). The PBAC previously considered a 0.5% reduction in HbA1c as suggested by the ESC was more relevant than the 0.3% proposed by in the November 2019 submission for a superiority claim. This outcome was not met in the comparison with dulaglutide 1.5 mg in SUSTAIN 7. (para 7.5, semaglutide PSD, November 2019 PBAC meeting).

5.8 Treatment with semaglutide 0.5 mg was associated with a statistically significant reduction in body weight compare with dulaglutide. More patients achieved weight loss of $\geq 5\%$ with semaglutide 0.5 mg compared with dulaglutide. The ESC previously considered that the mean difference of 3.55 kg in weight loss between semaglutide 1.0 mg and dulaglutide 1.5 mg may be clinically important (para 6.29, semaglutide PSD, November 2019 PBAC meeting). The PBAC previously considered the weight loss outcomes from the SUSTAIN trials in the context of how significant weight loss was specified in the regulatory draft guidance from the FDA¹. The PBAC previously noted that when using this suggested MCID for weight loss, in the comparisons against both exenatide 2.0 mg and dulaglutide 1.5 mg, semaglutide 1.0 mg provided a meaningful difference in the proportion of patients achieving $\geq 5\%$ weight loss by study end (56 weeks in SUSATIN 3 and 40 weeks in SUSTAIN 7). However, the sustainability of this weight loss and its translation into long-term clinical benefits remains unclear. (para 7.6, semaglutide PSD, November 2019 PBAC meeting)

Comparative harms

5.9 Overall safety data from the low and high dose arms for semaglutide and dulaglutide from the SUSTAIN 7 trial (40 weeks) are summarised in Table 4 below.

Table 4: Summary of key adverse events in the SUSTAIN 7 trial (on-treatment without rescue medication analysis)

Adverse event	Semaglutide 0.5 mg N=301		Dulaglutide 0.75 mg N=299		Semaglutide 1.0 mg N=300		Dulaglutide 1.5 mg N=299	
	n (%)	Rate / 100 patient- years	n (%)	Rate / 100 patient- years	n (%)	Rate / 100 patient- years	n (%)	Rate / 100 patient- years
Any adverse event	204 (68)	412.7	186 (62)	326.2	207 (69)	439.7	221 (74)	402.6
Serious adverse event	17 (6)	9.8	24 (8)	13.8	23 (8)	11.7	22 (7)	13.9
Discontinuation due to adverse event	24 (8)	19.7	14 (5)	9.4	29 (10)	28.6	20 (7)	21.5
Deaths	1 (<1)	0.4	2 (1)	0.8	1 (<1)	0.4	2 (1)	2.0
Adverse events of special interest								
GI adverse event	129 (43)	168.3	100 (33)	104.5	133 (44)	215.7	143 (48)	165.4
Injection-site reactions	4 (1)	2.1	4 (1)	3.7	6 (2)	2.6	8 (3)	7.2
Gallbladder disorders	2 (1)	0.9	4 (1)	1.6	4 (1)	2.2	8 (3)	3.8
Severe hypoglycaemia or blood glucose-confirmed symptomatic	2 (1)	1.3	3 (1)	1.2	5 (2)	3.0	5 (2)	2.1
Diabetic retinopathy	2 (1)	0.8	2 (1)	0.8	2 (1)	0.8	3 (1)	1.2

Source: Table 10, semaglutide Public Summary Document, November 2019 PBAC meeting

Abbreviation: GI, gastrointestinal

¹ Regulatory guidelines for weight management products suggest efficacy benchmarks after 1 year of treatment of either: statistically significant difference in weight loss of $\geq 5\%$ between arms; or the proportion of patients with $\geq 5\%$ weight loss is at least 35% in the intervention arm, is approximately double the proportion in the placebo arm, and the difference between arms is statistically significant (FDA Draft Guidance Feb 2007).

- 5.10 The PBAC previously considered that it was probable that a substantial number of patients would use 0.5 mg semaglutide in preference to the 1.0 mg strength due to the high gastrointestinal side effect profile of semaglutide 1.0 mg and the relatively high response rates to HbA1c and weight loss targets for semaglutide 0.5 mg (para 7.11, semaglutide PSD, November 2019 PBAC meeting).
- 5.11 The PBAC previously noted the availability of semaglutide in overseas markets could have provided some information on the proportion of use of the 0.5 mg versus 1 mg strength in clinical practice (para 7.11, semaglutide PSD, November 2019 PBAC meeting).
- 5.12 No additional information on overseas usage was provided in the resubmission.
- 5.13 The PBAC noted that adverse event rates were similar between semaglutide 0.5 mg and dulaglutide 1.5 mg.

Clinical claim

- 5.14 The resubmission claimed non-inferior comparative effectiveness and safety of semaglutide (0.5 mg and 1.0 mg) weekly compared with dulaglutide 1.5 mg weekly.
- 5.15 The PBAC has previously recommended that semaglutide 1.0 mg is non-inferior in terms of efficacy and safety compared to dulaglutide 1.5mg (para 6.64, semaglutide PSD, November 2019 PBAC meeting).
- 5.16 The ESC previously considered that semaglutide 0.5 mg once weekly was potentially non-inferior in terms of effectiveness and safety compared with dulaglutide 1.5 mg once weekly (para 6.63, semaglutide PSD, November 2019 PBAC meeting).
- 5.17 The PBAC previously noted that the effects of semaglutide compared to dulaglutide 1.5 mg are attenuated if not titrated to the maximum dose (1.0 mg). The PBAC considered that this was an important consideration due to the high gastrointestinal side effect profile of semaglutide 1.0 mg and that it was probable that a substantial number of patients will use semaglutide 0.5 mg in preference to the 1.0 mg strength due to the relatively high response rates to HbA1c and weight loss targets. (para 7.11, semaglutide PSD, November 2019 PBAC meeting).
- 5.18 The PBAC considered that the claim of non-inferior comparative effectiveness of semaglutide 0.5 mg to dulaglutide 1.5 mg was reasonable.
- 5.19 The PBAC considered that the claim of non-inferior comparative safety of semaglutide 0.5 mg to dulaglutide 1.5 mg was reasonable.

Economic analysis

- 5.20 The minor submission presented a cost-minimisation analysis of semaglutide compared with dulaglutide (para 7.4, semaglutide PSD, November 2019 PBAC meeting).

- 5.21 The submission argued that both strengths of semaglutide should be cost-minimised equally to dulaglutide 1.5mg once weekly in order to support a request for flat pricing across the two strengths of semaglutide. The previous submission also requested flat pricing for both strengths of semaglutide, however the PBAC did not consider that the proposal for the same price for both presentations of semaglutide was supported and pricing of the 0.5 mg dose of semaglutide would be determined by the Department according to usual methods (para 7.15, semaglutide PSD, November 2019 PBAC meeting)
- 5.22 The PBAC previously recommended that the equi-effective doses are as follows: when used in combination with metformin (dual therapy) and in combination with metformin plus a sulfonylurea (triple therapy) semaglutide 1.0 mg once weekly is equi-effective to dulaglutide 1.5 mg once weekly (para 7.4, semaglutide PSD, November 2019 PBAC meeting).

Drug cost/patient/year: \$ [REDACTED]

- 5.23 The estimated drug cost/patient/year would be \$ [REDACTED], based on effective DPMQ per script \$ [REDACTED] / 28 days per script x 365 day per year.

Estimated PBS usage & financial implications

- 5.24 The minor submission estimated there to be no financial implications to the PBS or changes in PBS usage as the submission expects semaglutide to only substitute for dulaglutide, to which it is cost minimised.

Table 5: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed semaglutide 2mg/1.5mL	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Number of scripts dispensed semaglutide 4mg/3mL	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Estimated financial implications of semaglutide						
Net cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Estimated financial implications for dulaglutide						
Net cost to PBS/RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Net financial implications						
Net cost to PBS/RPBS	\$0	\$0	\$0	\$0	\$0	\$0

Source: table 4, p11 of the resubmission

The redacted table shows that at Year 6, the estimated number of scripts dispensed for semaglutide 2 mg/1.5 mL to be 10,000 – 20,000 scripts; and semaglutide 4 mg/3 mL to be 50,000 – 100,000 scripts.

- 5.25 As a minor submission, the financial estimates have not been independently evaluated.

- 5.26 The PBAC recalled that 100,000 – 200,000 prescriptions for dulaglutide (June 2018 to May 2019) were dispensed in the first year of listing (para 6.100, semaglutide PSD, November 2019 PBAC meeting), and noted that the current estimate only allowed for 50,000 – 100,000 prescriptions for semaglutide in the first year of listing.
- 5.27 The PBAC also noted that since its previous consideration of semaglutide at the November 2019 meeting, the Australian Diabetes Society had revised its position statement on T2DM management to include GLP-1 therapies as second line add-on therapy.²

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended that semaglutide 0.5 mg should be considered equi-effective to dulaglutide 1.5 mg for treatment of patients with T2DM who have inadequate glycaemic control, as dual therapy in combination with metformin or a sulfonylurea where either of these is contraindicated or not tolerated; or triple therapy in combination with metformin and a sulfonylurea.
- 6.2 The PBAC recalled that it had previously accepted HbA1c differences of 0.3-0.4% as a non-inferiority margin in the context of non-inferiority claims. (para 6.11, semaglutide PSD, November 2019 PBAC meeting). The PBAC considered this outcome was met for semaglutide 0.5 mg in the comparison with dulaglutide 1.5 mg.
- 6.3 The PBAC considered that semaglutide 0.5 mg once weekly was non-inferior to dulaglutide 1.5 mg once weekly in terms of efficacy and safety.
- 6.4 The recommended equi-effective doses for the cost-minimisation to dulaglutide are as follows: when used in combination with metformin (dual therapy) and in combination with metformin plus a sulfonylurea (triple therapy) both semaglutide 0.5 mg once weekly and 1.0 mg once weekly are equi-effective to dulaglutide 1.5 mg once weekly. The PBAC considered flat pricing across the semaglutide doses was acceptable based on the acceptance of a non-inferior outcome for both doses.
- 6.5 The PBAC considered that the estimated use was likely to be a significant underestimate and that the financial model presented in the November 2019 submission was more informative. The PBAC recalled from November 2019, it considered that the estimated cost of listing semaglutide on the PBS was associated with significant uncertainties due to a substantially underestimated size and projected growth of the DPP4/SGLT2 inhibitor market, highly uncertain GLP-1 market dynamics, cost-offsets attributed to delay in insulin use and assumed substitution rates used to estimate cost-offsets. However, with the cost per patient of semaglutide the same as dulaglutide, the overall financial impact will be close to nil.

² <https://diabetessociety.com.au/documents/T2DManagementAlgorithm26022020.pdf>

- 6.6 The PBAC recommended that the restriction for listing should be the same as that recommended in November 2019.
- 6.7 The PBAC advised that semaglutide should be treated as interchangeable on an individual patient basis with dulaglutide and exenatide.
- 6.8 The PBAC advised that semaglutide is suitable for prescribing by nurse practitioners.
- 6.9 The PBAC recommended that the Early Supply Rule should not apply.
- 6.10 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new item (no change to the November 2019 recommended listing):

Name, Restriction, Manner of administration and form	PBS item code	Max. qty Packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer	
SEMAGLUTIDE						
1.34 mg/1 mL injection, 1 x 1.5 mL pen device	New	1	1	5	Ozempic®	Novo Nordisk
1.34 mg/1 mL injection, 1 x 3 mL pen device	New	1	1	5	Ozempic®	Novo Nordisk

Dual combination therapy:

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required - Streamlined
<p>Indication: Diabetes mellitus type 2</p> <p>Clinical criteria:</p> <ul style="list-style-type: none"> ▪ The treatment must be in combination with metformin; or ▪ The treatment must be in combination with a sulfonylurea <p>AND</p> <ul style="list-style-type: none"> ▪ Patient must have a contraindication to a combination of metformin and a sulfonylurea; or ▪ Patient must not have tolerated a combination of metformin and a sulfonylurea <p>AND</p> <ul style="list-style-type: none"> ▪ Patient must have, or have had, a HbA1c measurement greater than 7% prior to the initiation of a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 or a sodium-glucose co-transporter 2 (SGLT2) inhibitor despite treatment with either metformin or a sulfonylurea; or ▪ Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period prior to initiation with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor despite treatment with either metformin or a sulfonylurea
<p>Prescribing Instructions:</p> <p>The date and level of the qualifying HbA1c measurement must be, or must have been, documented in the patient's medical records at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor is initiated.</p> <p>The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor was initiated.</p> <p>Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances:</p> <p>(a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or</p> <p>(b) Had red cell transfusion within the previous 3 months.</p> <p>The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor, must be documented in the patient's medical records.</p>
<p>Administrative Advice:</p> <p>This drug is not PBS-subsidised for use as monotherapy or in combination with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), an insulin or an SGLT2 inhibitor.</p> <p>Special Pricing Arrangements apply.</p>

Triple combination therapy:

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required - Streamlined
<p>Indication: Diabetes mellitus type 2</p> <p>Clinical criteria:</p> <ul style="list-style-type: none"> ▪ The treatment must be in combination with metformin AND ▪ The treatment must be in combination with a sulfonylurea AND ▪ Patient must have, or have had, a HbA1c measurement greater than 7% prior to the initiation of a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 or a sodium-glucose co-transporter 2 (SGLT2) inhibitor despite treatment with maximally tolerated doses of metformin and a sulfonylurea; or ▪ Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period prior to initiation with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor despite treatment with maximally tolerated doses of metformin and a sulfonylurea
<p>Prescribing Instructions:</p> <p>The date and level of the qualifying HbA1c measurement must be, or must have been, documented in the patient's medical records at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor is initiated.</p> <p>The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor was initiated.</p> <p>Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances: (a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or (b) Had red cell transfusion within the previous 3 months.</p> <p>The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor, must be documented in the patient's medical records.</p>
<p>Administrative Advice:</p> <p>This drug is not PBS-subsidised for use as monotherapy or in combination with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), an insulin or an SGLT2 inhibitor.</p> <p>Special Pricing Arrangements apply.</p>

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.