

7.12 DULAGLUTIDE, Injection 1.5 mg in 0.5 mL single dose pre-filled pen, Trulicity[®], Eli Lilly Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor resubmission requested an Authority Required (STREAMLINED) listing for dulaglutide 1.5 mg once weekly (QW) for the treatment of type 2 diabetes mellitus (T2DM) in combination with insulin and metformin unless contraindicated or not tolerated.

2 Background

Registration status

- 2.1 An extension of the TGA indication for dulaglutide 1.5 mg QW to include use in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control, was approved by the TGA on 18 July 2019.

Previous PBAC consideration

- 2.2 The PBAC recommended dulaglutide 1.5 mg QW at its November 2017 meeting for the treatment of T2DM as dual therapy in combination with metformin, and triple therapy in combination with metformin and a sulfonylurea.
- 2.3 A major submission to extend the existing listing of dulaglutide QW to allow use in combination with insulin (and metformin, if not contraindicated or not tolerated) was considered by the PBAC at its November 2019 meeting.
- 2.4 Key outstanding matters of concern from the November 2019 meeting are summarised in the table below.

Table 1: Summary of key matters of concern in previous PBAC consideration

Matter of concern (November 2019)	How the resubmission addresses it
The PBAC considered that any price advantage applied should only account for the proportion of patients with high clinical needs who are likely to benefit from the simplified dosing regimen of dulaglutide QW (paragraph 7.8).	The sponsor maintained that the previously requested price advantage of \$■■■■ per week over exenatide BID was reasonable.
The PBAC considered that utilisation would be substantially higher than estimated due to underestimates in patient numbers, market share and market growth (paragraph 7.9).	Updated financial estimates to include uptake from other T2DM therapies in addition to exenatide BID.

Source: compiled by the Secretariat. Paragraph references refer to the November 2019 PBAC Public Summary Document.

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

3 Requested listing

- 3.1 The resubmission did not include a requested listing. It was assumed that no changes were proposed to the previously requested restriction which is consistent with the PBS listings of exenatide 5 mcg and 10 mcg BID for the same indication.

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

4 Comparator

- 4.1 The PBAC previously considered that exenatide 10 mcg BID was the appropriate main comparator.

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.

Economic analysis

- 5.3 The resubmission requested the same price advantage over exenatide BID as the November 2019 submission of \$[REDACTED] per week, which was incorporated as a cost offset in the previous cost-minimisation analysis. The price advantage was pragmatically determined as the difference between the cost of dulaglutide per week (\$[REDACTED]) and exenatide 10 mcg BID per week (\$17.02), accounting for the cost offset of reduced needles per week (\$[REDACTED]). The cost-minimisation presented in the November 2019 submission is shown below.

Public Summary Document – July 2020 PBAC Meeting

Table 2: Results of the cost-minimisation analysis in the previous submission

Component	Dulaglutide 1.5 mg QW	Exenatide 10 mcg BID
Cost per dose (AEMP)	\$ [REDACTED]	\$1.22
Dose frequency	Once weekly	Twice daily
Administrations per week	1	14
Total medicine cost per week	\$ [REDACTED]	\$17.02
Cost offset – needle use per week ^a	-	\$ [REDACTED]
Cost offset – adherence per week ^b	-	\$ [REDACTED]
Total health care costs per week	\$ [REDACTED]	\$ [REDACTED]

^a cost-offset for needle use per week was calculated based on the cost of 50% of the needles required for one week's supply (equivalent to the cost of 7 needles). The average cost for one needle was estimated at \$ [REDACTED], based on the average cost of needles from several Australian online diabetes supply stores (See Attachment A6.1 of the submission).

^b calculated as the difference between the cost (AEMP) of one week's treatment for exenatide 10 mcg twice daily and dulaglutide QW, minus the cost offset for needle use per week.

Source: Table 3.4.2, Table 3.4.3, p125 of the November 2019 submission

Abbreviations: AEMP: approved ex-manufacturer price

5.4 Despite the PBAC's previous advice that any requested price advantage over exenatide BID should be proportionate to the small number of high clinical need populations who may experience health benefits from likely improved adherence with dulaglutide QW, the resubmission maintained that the requested price advantage of \$ [REDACTED] per week was reasonable on the basis that the price advantage of exenatide 2 mg QW over exenatide 10 mcg BID is \$ [REDACTED] per week. The pre-PBAC response presented additional information to support the requested price advantage (see paragraphs 5.6 and 5.7 below) and utilised data from an Australian observational study (Haines et al.¹, 2016) in an alternative method to determine a price advantage for dulaglutide QW over exenatide BID. The pre-PBAC response noted that data from Haines et al., 2016 showed that the prevalence of T2DM in aged care facilities was 18.2% with 21.3% of those patients treated with insulin and 34.3% treated with oral antihyperglycaemic agents. Based on this data, the pre-PBAC response estimated that the population receiving insulin combination therapy is approximately 62% of the population receiving oral combination therapy and applying this relativity to the price advantage of dulaglutide QW over exenatide 10 mcg BID results in a price advantage of \$ [REDACTED]. The pre-PBAC response indicated the aged care population would constitute the majority of high clinical need populations compared to the Indigenous Australian or mental health populations and on this basis, considered that this price advantage could be applied across all high clinical need populations. The PBAC noted that Haines et al., 2016 was a small cross-sectional observational study of 107 patients in north-east Victorian aged care facilities with T2DM and 1 patient with Type 1 diabetes

¹ Haines, Helen M., Bannon Murphy, Holly., Amos, Tim., Kronos, Robert. "Prevalence and management of diabetes in residential aged care facilities in north-east Victoria, Australia", Volume 45, No.12, December 2016 Pages 908-911. Royal Australian College of General Practitioners 2016. REPRINTED FROM AFP VOL.45, NO.12, DECEMBER 2016

mellitus. The PBAC considered that Haines et al., 2016 did not provide a reliable basis for estimating the proportion of aged care patients treated with insulin given the data was based on a small number of patients and the study did not provide information on the proportion of patients receiving both insulin and oral agents.

- 5.5 While no direct evidence was provided to demonstrate the once weekly dosing regimen would result in better health outcomes for patients with high clinical needs, the resubmission stated that patients with high clinical needs referred to patients with comorbidities including cardiovascular and kidney diseases, microvascular complications, serious mental illness; as well as socio-economic disadvantage and specific challenges in disease management (e.g. Indigenous Australians). The resubmission indicated that most patients treated with a glucagon-like peptide-1 receptor agonist (GLP-1 RA) in combination with insulin would be on third or later line therapy and could be considered to be in high clinical need, given these patients are likely to require specialist endocrinology consultation due to increased clinical complexity. The resubmission noted that the most recent Australian Type 2 Diabetes management algorithm (Australian Diabetes Society, 2020) also positions GLP-1 RA in combination with insulin as third or later line therapy. The PBAC considered that mostly general practitioners rather than endocrinologists would manage the addition of dulaglutide QW, for patients already on insulin therapy.
- 5.6 The pre-PBAC response presented data from two retrospective observational studies (Mody et al.², 2019; Mody et al.³, 2020) as evidence for improved adherence with dulaglutide QW compared to other GLP-1 RAs. The pre-PBAC response noted that the results from Mody et al., 2019 indicated there was higher adherence to treatment amongst patients receiving dulaglutide compared to patients receiving liraglutide, exenatide BID or exenatide QW and the adherence advantage of dulaglutide was replicated in Mody et al., 2020 where adherence with dulaglutide was higher compared to semaglutide and exenatide QW.
- 5.7 The pre-PBAC response maintained that most patients treated with a GLP-1 RA in combination with insulin would likely have high clinical needs given the nature of disease progression. The pre-PBAC response presented advice from the Chair of the Diabetes Specific Interest Network of the Royal Australian College of General Practitioners that “patients initiated on insulin versus those on oral or non-insulin combinations are identified as being older, at increased risk of micro and macro vascular complications and having higher rates of multi-morbid conditions.” The pre-PBAC response also noted that an analysis of 21,531 patients of Kaiser Permanente

² Mody R, Huang Q, Yu M, et al. Adherence, persistence, glycaemic control and costs among patients with type 2 diabetes initiating dulaglutide compared with liraglutide or exenatide once weekly at 12-month follow-up in a real-world setting in the United States. *Diabetes Obes Metab.* 2019;1–10. <https://doi.org/10.1111/dom.13603>

³ Mody et al Dulaglutide Has Higher Adherence and Persistence than Semaglutide and Exenatide QW: 6 month follow up from US real Word Data, American Diabetes Association 80th Annual Scientific Sessions, Chicago, IL; June 12-16 2020 (P-928)

Electronic Health Data (Weiner JZ et al.⁴, 2019) showed that insulin use at 75 years of age was higher in individuals with poor health (pulmonary, cardiac or renal disease; diagnosis of dementia; or metastatic cancer) compared to those with good health, and the likelihood of continued insulin use was higher among individuals with poor health.

Estimated PBS usage & financial implications

5.8 The previous submission estimated the number of patients utilising dulaglutide with insulin to be 500 to < 5,000 patients in Year 1 increasing to 5,000 to < 10,000 patients in Year 6, based on the size of the existing market for exenatide BID with insulin. The PBAC previously considered the estimated financial impact of extending the current listing of dulaglutide to include use in combination with insulin was substantially underestimated noting there were 281,419 patients with T2DM requiring insulin therapy registered with the National Diabetes Services Scheme (NDSS) in 2019. The resubmission contended that data from the NDSS overestimated the eligible population as it contained patients more likely to have complex disease or from lower socio-economic groups that generally have poorer health and higher rates of comorbidities that would necessitate use of more complex regimens such as insulin. The resubmission further noted that the NDSS data did not account for non-adherence or persistence to insulin. As such, the resubmission maintained that the approach used to estimate the number of patients that would use dulaglutide QW in combination with insulin in November 2019 was appropriate.

5.9 The resubmission updated the financial estimates to include uptake from other T2DM therapies in addition to exenatide BID. The key inputs into the revised financial estimates are summarised in the Table 3 below.

Table 3: Changes to key inputs in the financial estimates

Parameter	November 2019 major submission	July 2020 Proposal	Comment
Market size			
Estimated use of dulaglutide in combination with insulin	The market size of dulaglutide with insulin was estimated based on the existing market for exenatide (5 mcg or 10 mcg) BID with insulin using a 10% sample of PBS data from October 2015 to December 2018.	The estimated market size for dulaglutide with insulin was revised to included substitution of exenatide QW, SGLT2 and DPP-4 inhibitor use based on an analysis of a 10% sample of PBS data from October 2015 to December 2019.	The same market share approach as the November 2019 submission was used to estimate the market size, using a 10% sample of PBS data extrapolated over the 6 years of listing with the same assumption that patients were on treatment if a script was refilled within a 6 month period.
Patient numbers/Market share			

⁴ Weiner JZ et. al., Use and Discontinuation of Insulin Treatment Among Adults Aged 75 to 79 Years With Type 2 Diabetes, JAMA Intern Med. 2019;179(12):1633-1641]

Public Summary Document – July 2020 PBAC Meeting

Parameter	November 2019 major submission	July 2020 Proposal	Comment
Number of patients treated with exenatide BID (5 mcg + 10 mcg) (Uptake rate of dulaglutide)	<p>Year 1 (2020): 5,000 to < 10,000 (35%)</p> <p>Year 2 (2021): 5,000 to < 10,000 (55%)</p> <p>Year 3 (2022): 5,000 to < 10,000 (63%)</p> <p>Year 4 (2023): 5,000 to < 10,000 (68%)</p> <p>Year 5 (2024): 5,000 to < 10,000 (72%)</p> <p>Year 6 (2025): 5,000 to < 10,000 (76%)</p>	<p>Year 1 (2021): 5,000 to < 10,000 (35%)</p> <p>Year 2 (2022): 5,000 to < 10,000 (55%)</p> <p>Year 3 (2023): 5,000 to < 10,000 (63%)</p> <p>Year 4 (2024): 5,000 to < 10,000 (68%)</p> <p>Year 5 (2025): 5,000 to < 10,000 (72%)</p> <p>Year 6 (2026): 5,000 to <10,000 (76%)</p> <p>The resubmission indicated that patients who are adequately controlled with exenatide BID (with insulin) are less likely to switch to dulaglutide (with insulin).</p>	The estimated uptake rates of dulaglutide from exenatide BID were unchanged despite the PBAC's advice that the majority of patients receiving treatment with exenatide BID and insulin would switch to dulaglutide QW.
Number of patients treated with exenatide QW (Uptake rate of dulaglutide)	Not included	<p>Year 1 (2021): 500 to < 5,000 (25%)</p> <p>Year 2 (2022): 500 to < 5,000 (35%)</p> <p>Year 3 (2023): 500 to < 5,000 (50%)</p> <p>Year 4 (2024): 500 to < 5,000 (63%)</p> <p>Year 5 (2025): 500 to < 5,000 (68%)</p> <p>Year 6 (2026): 500 to < 5,000 (70%)</p>	Exenatide QW is not currently PBS listed for use with insulin. The resubmission claimed that the 10% sample of PBS data showed some use of exenatide QW with insulin (approx. 10% of exenatide QW usage). As such, the resubmission assumed that dulaglutide would replace exenatide for new patients initiating GLP-1 RA therapy in line with the proportion of current use.
Number of patients treated with SGLT2 inhibitors (Uptake rate# of dulaglutide) (pooled SGLT2 inhibitors: dapagliflozin, empagliflozin, and ertugliflozin)	Not included	<p>Year 1 (2021): 20,000 to < 30,000(5%)</p> <p>Year 2 (2022): 20,000 to < 30,000 (7%)</p> <p>Year 3 (2023): 20,000 to < 30,000 (9%)</p> <p>Year 4 (2024): 20,000 to < 30,000 (10%)</p> <p>Year 5 (2025): 20,000 to < 30,000 (12%)</p>	The resubmission considered that displacement of SGLT2 inhibitors by dulaglutide would be limited, as the role of SGLT2 inhibitors have become more distinguishable with the updated Australian Type 2 Diabetes management algorithm, which recommends use for patients with cardiovascular disease, heart failure or chronic kidney disease.

Public Summary Document – July 2020 PBAC Meeting

Parameter	November 2019 major submission	July 2020 Proposal	Comment		
		Year 6 (2026): 20,000 to < 30,000 (15%)			
Number of patients treated with pooled DPP-4 (Uptake rate# of dulaglutide) (pooled DPP-4 inhibitors: alogliptin, linagliptin, saxagliptin, sitagliptin, and vildagliptin)	Not included	Year 1 (2021): 20,000 to < 30,000 (10%) Year 2 (2022): 20,000 to < 30,000 (15%) Year 3 (2023): 20,000 to < 30,000 (18%) Year 4 (2024): 20,000 to < 30,000 (23%) Year 5 (2025): 20,000 to < 30,000 (23%) Year 6 (2026): 20,000 to < 30,000 (23%)	The resubmission considered that displacement of DPP-4 inhibitors by dulaglutide would be limited as DPP-4 inhibitors have demonstrated no benefits with respect to cardiovascular, heart failure or chronic kidney disease.		
Market growth					
November 2019	1% per annum				
July 2020	Exenatide BID	Exenatide QW	Pooled SGLT2	Pooled DPP-4	Comments
Year 1 (2021)	-1%	3%	5%	4%	Sensitivity analyses provided in Table 5.
Year 2 (2022)	-1%	2%	3%	3%	
Year 3 (2023)	-1%	1%	3%	2%	
Year 4 (2024)	0%	1%	2%	2%	
Year 5 (2025)	0%	1%	2%	2%	
Year 6 (2026)	-0.4%	1%	2%	1%	

Abbreviation: GLP-1 RA: glucagon-like peptide-1 receptor agonist; SGLT2 inhibitor: sodium-glucose co-transporter-2 inhibitor; DPP-4 inhibitor: dipeptidyl peptidase-4 inhibitor ('gliptin')

Note: the resubmission estimated the number of patients (with insulin) in the absence of a dulaglutide listing, using a 10% sample of PBS data extrapolated over the 6 years of listing.

Uptake rates for SGLT2 and DPP-4 were estimated based on a 10% sample of PBS data from June 2006 to December 2019 of patients who switched from SGLT2 or DPP-4 to a GLP-1 RA. 14% had received an SGLT2 and 43% had received a DPP4 prior to receiving exenatide BID during that time period.

Source: compiled by the Secretariat, pp4-16, Table 2, p9 of the minor resubmission; Dulaglutide Section 4 Model_April 2020.xlsx

5.10 The PBAC previously considered that the majority of prescribers would likely substitute exenatide BID with dulaglutide QW in patients currently treated with exenatide BID in combination with insulin given the more convenient dosing schedule (paragraph 7.9, dulaglutide Public Summary Document (PSD), November 2019). However, the sponsor considered that patients who are adequately controlled with exenatide BID (with insulin) are less likely to switch to dulaglutide QW (with insulin) thus the estimated uptake rates of dulaglutide QW from exenatide BID were unchanged in the resubmission (see Table 3). The sponsor indicated in the

Public Summary Document – July 2020 PBAC Meeting

resubmission that the uptake rates presented in the previous submission were likely an overestimation, however presented the same uptake rates. The pre-PBAC response noted the uptake rate of dulaglutide QW from exenatide BID applied in the estimates at 61.5% over the first 6 years of listing was substantially higher than the uptake rate of 40.3% previously accepted by the PBAC for dulaglutide QW in November 2017. The pre-PBAC response also noted that the displacement rates of exenatide BID for dulaglutide QW in the oral combination market were 16.4% and 29.5% in Years 1 and 2 of listing which were lower than the uptake rates from the exenatide BID market applied in the resubmission (35% in Year 1 and 55% in Year 2).

- 5.11 The resubmission used a pragmatic approach to derive the estimates of utilisation from displacement of SGLT2 and DPP-4 inhibitors, where pooled data from all DPP-4/SGLT2 inhibitors listed on the PBS were included.
- 5.12 Semaglutide QW was recommended by the PBAC for the treatment of patients with T2DM who have inadequate glycaemic control, in combination with metformin and/or a sulfonylurea where either of these is contraindicated or not tolerated in November 2019. This may impact on the uptake of dulaglutide QW.
- 5.13 The PBAC previously considered that the dulaglutide market would likely grow beyond estimated (1% per annum), noting the changes in clinical place for GLP-1 RA therapies (paragraphs 7.9, dulaglutide PSD, November 2019). The resubmission noted expert advice indicated that patients with T2DM are most likely to be treated with oral combination therapy prior to initiating injectable therapy in clinical practice. However, the resubmission considered that if GLP-1 RA therapies are used earlier, consistent with current clinical guidelines, this would mainly increase utilisation of GLP-1 RAs without insulin as it remains as a later line of therapy in the treatment pathway. Whilst early use of GLP-1 RAs may contribute to delay in a combination of dulaglutide and insulin, the market size and projected growth for dulaglutide QW are associated with high uncertainties due to increasing complexity in the management of T2DM and uncertain GLP-1 RA market dynamics. The PBAC previously considered that use of dulaglutide QW in combination with SGLT2 inhibitors outside the current PBS restrictions was likely due to cardiovascular benefits, lower risk of hypoglycaemia and weight loss benefits (paragraph 7.10, dulaglutide PSD, November 2019).
- 5.14 Revised estimates shown in Table 4 below indicate the net cost to the PBS/RPBS in Year 1 (2021) is \$0 to < \$10 million, increasing to \$0 to < \$10 million in Year 6 (2026) with a total net cost to the PBS/RPBS of \$30 million < \$40 million over the first 6 years of listing where the proposed price advantage for dulaglutide over exenatide BID was unchanged.

Table 4: Estimated use and financial implications

	Year 1 (2021)	Year 2 (2022)	Year 3 (2023)	Year 4 (2024)	Year 5 (2025)	Year 6 (2026)
Estimated utilisation of dulaglutide from exenatide 5 mcg and 10 mcg twice daily (with insulin) market						

Public Summary Document – July 2020 PBAC Meeting

	Year 1 (2021)	Year 2 (2022)	Year 3 (2023)	Year 4 (2024)	Year 5 (2025)	Year 6 (2026)
Number of patients treated with exenatide BID in absence of dulaglutide	████	████	████	████	████	████
Estimated uptake rate of dulaglutide (displacement of exenatide BID)	35%	55%	63%	68%	72%	76%
Number of scrip substituted by dulaglutide	-████	-████	-████	-████	-████	-████
Cost to PBS/RPBS less copayments ^a displaced from exenatide BID market	-\$████	-\$████	-\$████	-\$████	-\$████	-\$████
Estimated utilisation of dulaglutide from exenatide 2 mg once weekly (with insulin) market						
Number of patients treated with exenatide QW in absence of dulaglutide	████	████	████	████	████	████
Estimated uptake rate of dulaglutide (displacement of exenatide QW)	25%	35%	50%	63%	68%	70%
Number of scripts substituted by dulaglutide	-████	-████	-████	-████	-████	-████
Cost to PBS/RPBS less copayments ^b displaced from exenatide QW market	-\$████	-\$████	-\$████	-\$████	-\$████	-\$████
Estimated utilisation of dulaglutide from SGLT2 inhibitors (with insulin) market						
Number of patients treated with pooled SGLT2 inhibitors in absence of dulaglutide	████	████	████	████	████	████
Estimated uptake rate of dulaglutide (displacement of SGLT2 inhibitors)	5%	7%	9%	10%	12%	15%
Number of scripts substituted by dulaglutide	-████	-████	-████	-████	-████	-████
Cost to PBS/RPBS less copayments ^c displaced from SGLT2 inhibitors market	-\$████	-\$████	-\$████	-\$████	-\$████	-\$████
Estimated utilisation of dulaglutide from DPP-4 inhibitors (with insulin) market						
Number of patients treated with DPP-4 inhibitors in absence of dulaglutide	-████	-████	-████	-████	-████	-████
Estimated uptake rate of dulaglutide (displacement of DPP-4 inhibitors)	10%	15%	18%	23%	23%	23%

Public Summary Document – July 2020 PBAC Meeting

	Year 1 (2021)	Year 2 (2022)	Year 3 (2023)	Year 4 (2024)	Year 5 (2025)	Year 6 (2026)
Number of scripts substituted by dulaglutide	- [REDACTED]	- [REDACTED]	- [REDACTED]	- [REDACTED]	- [REDACTED]	- [REDACTED]
Cost to PBS/RPBS less copayments ^d displaced from DPP-4 inhibitors market	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Estimated financial implications for the substituted medicines						
Total number of patients treated in absence of dulaglutide	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Total number of scripts substituted by dulaglutide	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Total cost to PBS/RPBS (effective) excluding copayments displaced by dulaglutide	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Estimated utilisation of dulaglutide (with insulin)						
Number of patients treated with dulaglutide QW	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Number of scripts dispensed	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Cost to PBS/RPBS less copayments ^{e,f}	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to the PBS/RPBS						
Net cost (effective) excluding copayments	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost (effective) excluding copayments from November 2019 submission	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

Note: Scripts per patient per year were 13.04 for dulaglutide; 12.18 for exenatide BID, exenatide QW, and pooled SGLT2; 13.04 for pooled DPP-4 and assuming 100% compliance.

^a Exenatide 5 mcg DPMQ \$66.39; 10 mcg DPMQ \$89.93

^b Exenatide QW DPMQ: \$131.30

^c Pooled SGLT2 inhibitors weighted average DPMQ: \$59.73

^d Pooled DPP-4 inhibitors weighted average DPMQ: \$55.31

^e Dulaglutide effective DPMQ: \$ [REDACTED]

^f A minor calculation error in Table 6 of the submission. The corrected estimates are presented as per '3c. Impact - EFF' in Section 4 workbook.

Source: Dulaglutide Section 4 Model_April 2020.xlsx

The redacted table shows the following estimates at Year 6:

- *Number of patients treated with exenatide BID in absence of dulaglutide was 5,000 to < 10,000 and number of scripts substituted by dulaglutide for this group was 50,000 to < 60,000;*
- *Number of patients treated with exenatide QW in absence of dulaglutide was 500 to < 5,000 and number of scripts substituted by dulaglutide for this group was 10,000 to < 20,000;*

Public Summary Document – July 2020 PBAC Meeting

- Number of patients treated with pooled SGLT2 inhibitors in absence of dulaglutide was 20,000 to < 30,000 and number of scripts substituted by dulaglutide for this group was 50,000 to < 60,000; Number of patients treated with DPP-4 inhibitors in absence of dulaglutide was 20,000 to < 30,000 and number of scripts substituted by dulaglutide for this group was 70,000 to < 80,000;
- Total number of patients treated in absence of dulaglutide was 60,000 to < 70,000 and total number of scripts substituted by dulaglutide for this group was 100,000 to < 200,000;
- Number of patients treated with dulaglutide QW was 10,000 to < 20,000 and the number of scripts dispensed was 200,000 to < 300,000;
- Net cost (effective) excluding copayments was \$0 to < \$10 million and net cost (effective) excluding copayments from November 2019 submission was \$0 to < \$10 million.

5.15 The resubmission presented results of sensitivity analyses (Table 5) to evaluate the impact of variable changes on the financial estimates. The variables tested included the use of a linear trend line to extrapolate exenatide BID, SGLT2, DPP4 inhibitors, and exenatide QW utilisation, increasing growth rates of patients treated with insulin across the nominated therapies, and increasing dulaglutide market share from baseline estimates. Results of the sensitivity analyses indicated that the financial estimates are likely to be sensitive to changes in these variables.

Table 5: Sensitivity Analyses to evaluate the impact of the financial estimates

	Year 1 (2021)	Year 2 (2022)	Year 3 (2023)	Year 4 (2024)	Year 5 (2025)	Year 6 (2026)
Base case	████████	████████	████████	████████	████████	████████
Linear trend line (\$)	████████	████████	████████	████████	████████	████████
Increased exenatide growth rate (\$) (3% year on year)	████████	████████	████████	████████	████████	████████
Increased SGLT2 & DPP4 growth rate (\$) (double historic trend)	████████	████████	████████	████████	████████	████████
Increased dulaglutide market share (\$)	████████	████████	████████	████████ 	████████ 	████████
Increased growth rates & market share (\$)	████████	████████	████████	████████ 	████████ 	████████

Note: sensitivity analyses were performed based on dulaglutide effective DPMQ: \$ ██████████
 Abbreviation: SGLT2 inhibitor: sodium-glucose co-transporter-2 inhibitor; DPP-4 inhibitor: dipeptidyl peptidase-4 inhibitor
 Source: Table 12, p16 of the submission

The redacted table shows financial estimates in the range of \$0 to < \$10 million and \$10 million to < \$20,000 million.

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

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

6 PBAC Outcome

- 6.1 The PBAC recommended extending the existing listing of dulaglutide to include the treatment of T2DM in combination with insulin and metformin unless contraindicated or not tolerated. The PBAC's recommendation for listing was based on, among other matters, its assessment, that the cost-effectiveness of dulaglutide 1.5 mg once weekly (QW) under the requested restriction would be acceptable if it were cost-minimised against exenatide 10 mcg twice daily (BID).
- 6.2 The PBAC considered that the QW dosing regimen of dulaglutide may improve health outcomes for some patients with high clinical needs, particularly those with poor adherence, due to less frequent injections compared with exenatide BID.
- 6.3 The PBAC noted that the resubmission requested the same price advantage per week over exenatide BID as the previous submission (\$■■■■) despite its previous advice that any price advantage applied should only account for the proportion of patients with high clinical needs who are likely to benefit from the simplified dosing regimen of dulaglutide QW. The PBAC noted that the resubmission indicated that most T2DM patients who would be treated with dulaglutide in combination with insulin could be classified as having high clinical needs on the basis that these patients are likely to have comorbidities and require specialist management due to high clinical complexity. The PBAC considered there was a distinction between patients with comorbidities and patients with high clinical needs who would derive benefit from likely improved adherence with dulaglutide QW.
- 6.4 The PBAC noted that the pre-PBAC response provided an alternative method for determining a price advantage for dulaglutide QW based on the estimated proportion of T2DM patients in aged care facilities receiving insulin combination therapy (see paragraph 5.4). The PBAC noted that the alternative price advantage of \$■■■■ was determined by applying the estimated proportion of aged care facility patients treated with insulin combination therapy relative to the proportion of patients treated with oral therapies (62%) using data from Haines et al., 2016, to the pricing advantage of exenatide QW over exenatide BID (\$■■■■). The PBAC considered that Haines et al., 2016 was not a reliable basis to determine a reasonable price advantage for dulaglutide QW due to the issues noted in paragraph 5.4. Irrespective of these issues, the PBAC considered that dulaglutide QW was unlikely to confer additional benefits from improved adherence to T2DM patients in aged care facilities, as staff would usually administer injectable therapy. While the PBAC considered that the patients who would benefit from likely improved adherence with dulaglutide QW are a

Public Summary Document – July 2020 PBAC Meeting

subpopulation of all T2DM patients with comorbidities, the PBAC acknowledged it may be difficult to estimate the size of this subpopulation. As such, the PBAC advised it would be reasonable if the current price advantage that dulaglutide QW has over exenatide 10 mcg BID was applied to this extended listing.

- 6.5 The PBAC maintained that exenatide BID was the appropriate comparator.
- 6.6 The PBAC recalled it previously considered that dulaglutide QW was non-inferior to exenatide BID in terms of comparative effectiveness and safety, and the equi-effective doses are dulaglutide 1.5 mg QW and exenatide 10 mcg BID.
- 6.7 The PBAC recalled it previously considered that a cost-offset for reduced needle use in the cost-minimisation analysis, based on 50% of the needle costs for one week's supply, was reasonable.
- 6.8 The PBAC noted the resubmission presented revised financial estimates to address its previous concerns that utilisation of dulaglutide in combination with insulin was underestimated. The PBAC noted that the revised estimated number of patients utilising dulaglutide in combination with insulin was 5,000 to < 10,000 patients in Year 1 increasing to 10,000 to < 20,000 patients in Year 6. The PBAC noted that the resubmission adopted a market share approach using a 10% sample of PBS data and that the revised estimates also included estimates of uptake from patients who would otherwise be treated with SGLT2 inhibitors, DPP-4 inhibitors, and exenatide 2 mg QW in addition to uptake from patients treated with exenatide 5 mcg and 10 mcg BID.
- 6.9 The PBAC affirmed that the majority of patients receiving exenatide BID would switch to dulaglutide QW if it becomes available on the PBS, due to less frequent injections compared with exenatide BID and noted the uptake rates of dulaglutide QW for exenatide BID as an add-on to oral therapies (metformin and/or a sulfonylurea) were lower than the estimated uptake rates for use with insulin (see paragraph 5.11). While the PBAC considered there was some remaining uncertainty around the estimated utilisation given the changing GLP-1 RA market (e.g. the listing of semaglutide), the PBAC considered that overall, the revised utilisation of dulaglutide QW in combination with insulin was reasonable.
- 6.10 The PBAC recommended that the restriction for the requested listing should be consistent with the current listings of exenatide 5 mcg and 10 mcg BID for the same indication.
- 6.11 The PBAC, noting that its recommendation was on a cost-minimisation basis, advised that as dulaglutide was not expected to provide a substantial and clinically relevant improvement in efficacy or a reduction in toxicity over exenatide BID and not expected to address a high and urgent unmet clinical need, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 6.12 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 restriction to dulaglutide (11364D) as follows:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
Dulaglutide 1.5 mg per 0.5 mL solution for injection, 4 x 1.5 mg single use pen (auto-injector)	1	5	Trulicity®, Eli Lilly Australia
Category/Program:	Authority Required (STREAMLINED)		
PBS indication:	Diabetes mellitus type 2		
Clinical criteria:	<p>The treatment must be in combination with insulin, AND</p> <p>The treatment must be in combination with metformin unless contraindicated or not tolerated, AND</p> <p>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 insulin and oral antidiabetic agents, or insulin alone where metformin is contraindicated; 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 insulin and oral antidiabetic agents, or insulin alone where metformin is contraindicated.</p>		
Prescriber Instructions:	<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>		
Administrative Advice:	<p>This drug is not PBS-subsidised for use as monotherapy or in combination with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), 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.