Semaglutide: analysis of utilisation

Drug utilisation sub-committee (DUSC)

June 2024

Abstract

Purpose

To review the utilisation of PBS listed semaglutide for the treatment of type 2 diabetes mellitus (T2DM), as requested by DUSC at its February 2024 meeting. The review also considered the utilisation of semaglutide in context with other glucagon-like peptide 1 (GLP-1) analogues.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Dulaglutide was PBS listed on 1 June 2018 and semaglutide was PBS listed on 1 July 2020.

Data Source / methodology

Data extracted from the PBS database maintained by the Department of Health and Aged Care, processed by Services Australia were used for the analyses. Prescription data were extracted from 1 January 2016 up to and including 31 December 2023 based on the date of supply. Patients who were only supplied insulin in this period were excluded as they were likely to be patients with type 1 diabetes.

Key Findings

- In 2023 there were approximately 1.6 million patients supplied one or more medicines through the PBS for T2DM, and 325,993 patients who were supplied semaglutide or dulaglutide, and 120,374 initiators to semaglutide or dulaglutide. Of the 120,374 initiators to either semaglutide or dulaglutide, 94% (113,058) were supplied semaglutide, compared to 6% (7,316) who were supplied dulaglutide.
- In 2023 there were 1,989,952 prescriptions of semaglutide supplied to 292,848 patients, and 404,703 prescriptions of dulaglutide were supplied to 80,576 patients.
- Due to the medicine shortages of semaglutide and dulaglutide, 12,330 patients initiated these medicines in the fourth quarter of 2022, compared to 32,648 in the fourth quarter of 2021.
- There were 16,077 patients who initiated a flozin or a gliptin after treatment with semaglutide or dulaglutide in the fourth quarter of 2022, compared with 4,574 patients in the fourth quarter of 2021.
- Of the patients who initiated onto therapy in 2018, 46% were initiated by GPs and 50% of patients were initiated by Endocrinology or Internal Medicine specialists. Of the

patients who initiated onto therapy in 2023, 81% were initiated by GPs and 13% of patients were initiated by Endocrinology or Internal Medicine specialists.

Purpose of analysis

To review the utilisation of PBS listed semaglutide for the treatment of type 2 diabetes mellitus (T2DM), as requested by DUSC at its February 2024 meeting. The review also considered the utilisation of semaglutide in context with other glucagon-like peptide 1 (GLP-1) analogues.

Background

Clinical situation

Diabetes mellitus is a condition where your pancreas does not produce enough insulin to control the level of sugar in your blood or, your body is not able to use the insulin it makes properly. In T2DM, the response to insulin is diminished, and this is defined as insulin resistance. During this state, insulin is ineffective and is initially countered by an increase in insulin production to maintain glucose homeostasis, but over time, insulin production decreases, resulting in T2DM. T2DM is most commonly seen in persons older than 45 years. It is increasingly seen in children, adolescents, and younger adults due to rising levels of obesity, physical inactivity, and energy-dense diets.[1]

GLP-1s are a class of medicines used to treat T2DM. This class of medicines includes semaglutide, dulaglutide, exenatide, lixisenatide, liraglutide and albiglutide.[2] Semaglutide and dulaglutide are the GLP-1s currently listed on the PBS. Exenatide was delisted from the PBS on 1 February 2023.

The TGA reported a shortage of semaglutide from 15 April 2022 due to an unexpected increase in consumer demand for its off-label use for weight loss, and shortage of dulaglutide from 27 June 2022 related to the shortage of semaglutide. As of May 2024, both shortages reported limited availability and a supply impact date until 31 December 2024.[3]

Pharmacology

GLP-1s help T2DM patients by mimicking the effects of a hormone called glucagon-like peptide 1 which is produced in the body when eating. When blood sugar levels start to rise after a patient with T2DM eats, GLP-1s stimulate the pancreas to secrete insulin and reduce blood glucose levels.[4]

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[1] Goyal R, Singhal M, Jialal I. Type 2 Diabetes. [Updated 2023 Jun 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513253/

[2] Collins L, Costello RA. Glucagon-Like Peptide-1 Receptor Agonists. [Updated 2023 Jan 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551568/

[3] The Department of Health and Aged Care, Therapeutic Goods Administration, Medicine shortage reports database, accessed 2 May 2024 https://apps.tga.gov.au/Prod/msi/Search/Index?shortagetype=All

[4] Andreasen CR, Andersen A, Knop FK, Vilsbøll T. How glucagon-like peptide 1 receptor agonists work. Endocr Connect. 2021 Jul 17;10(7):R200-R212. doi: 10.1530/EC-21-0130. PMID: 34137731; PMCID: PMC8346189.

Therapeutic Goods Administration (TGA) approved indications

Semaglutide is indicated for the 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.

Semaglutide is subject to additional monitoring in Australia under the black triangle scheme.[5]

Dulaglutide is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with T2DM:

- As monotherapy.
- In combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

Dulaglutide is indicated as an adjunct to standard of care therapy to reduce the risk of major adverse cardiovascular events in adults with T2DM who have:

- established cardiovascular disease or
- multiple cardiovascular risk factors.[6]

Dosage and administration

Semaglutide

Semaglutide starting dose is 0.25 mg once weekly. After 4 weeks, the dose should be increased to 0.5 mg once weekly. After at least 4 weeks with a dose of 0.5 mg once weekly, the dose can be increased to 1 mg once weekly to further improve glycaemic control.

Semaglutide 0.25 mg is not a maintenance dose.

When semaglutide is added to existing metformin and/or thiazolidinedione therapy, the current dose of metformin and/or thiazolidinedione can be continued unchanged.

When semaglutide is added to existing therapy of a sulfonylurea or insulin, a reduction in the dose of sulfonylurea or insulin should be considered to reduce the risk of hypoglycaemia.[5]

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[5] (Ozempic) semaglutide Australian Approved Product Information. North Sydney: Novo Nordisk Pharmaceuticals Pty Limited. Approved 28 August 2019, updated 26 October 2023. Available from https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2019-PI-01881-1&d=20240507172310101

[6] (Trulicity) dulaglutide Australian Approved Product Information. Sydney: Eli Lilly Australia Pty. Ltd. Approved 19 January 2015, updated 8 May 2023. Available fromhttps://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2015-PI-01412-1

Dulaglutide

Dulaglutide should be administered once weekly. The dose can be administered at any time of the day, with or without meals, and can be injected subcutaneously in the abdomen, thigh or upper arm. Dulaglutide should not be administered intravenously or intramuscularly. Dulaglutide is for single use in one patient only. The pen is discarded once the injection is completed.

The recommended dose of dulaglutide in adults (≥ 18 years) is 1.5 mg per week. Dulaglutide is administered once weekly, at any time of day, independently of meals.

No dose adjustment is required based on age in patients over the age of 65 years.

The safety and effectiveness of dulaglutide have not been established in children and adolescents under 18 years of age.[6]

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from the TGA (Product Information) and the TGA (Consumer Medicines Information).

PBS listing details (as at 1 May 2024)

Table 1: PBS listing of semaglutide

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
12075M	semaglutide 1.34 mg/mL injection, 1 x 3 mL pen device	1	5	$133.80	Ozempic Novo Nordisk Pharmaceuticals Pty. Limited
12080T	semaglutide 1.34 mg/mL injection, 1 x 1.5 mL pen device	1	5	$133.80	Ozempic Novo Nordisk Pharmaceuticals Pty. Limited

Source: the PBS website. Special Pricing Arrangements apply.

Table 2: PBS listing of dulaglutide

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
11364D	dulaglutide 1.5 mg/0.5 mL injection, 4 x 0.5 mL pen devices	4	5	$133.80	Trulicity Eli Lilly Australia Pty Ltd

Source: the PBS website. Special Pricing Arrangements apply.

Restriction

Semaglutide and dulaglutide are PBS listed for T2DM.

- The treatment must be in combination with metformin; or the treatment must be in combination with a sulfonylurea, AND
  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.
- The treatment must be in combination with metformin, AND the treatment must be in combination with a sulfonylurea.
- The treatment must be in combination with insulin, AND the treatment must be in combination with metformin unless contraindicated or not tolerated.

For additional criteria including HbA1c or blood glucose measurements, the full wording of the restriction, and the current PBS listing refer to the PBS website.

Date of listing on PBS

Dulaglutide was PBS listed on 1 June 2018 and semaglutide (Ozempic) was PBS listed on 1 July 2020.

Changes to listing

Table 3: Summary of changes to the PBS listing of GLP-1s

Change to the PBS	Date of change
Exenatide PBS listed	1 August 2010
Dulaglutide PBS listed either in combination with metformin and a sulfonylurea or to treat patients with a contraindication to a combination of metformin and a sulfonylurea or who could not tolerate a combination of metformin and a sulfonylurea	1 June 2018
Semaglutide PBS listed either in combination with metformin and a sulfonylurea or to treat patients with a contraindication to a combination of metformin and a sulfonylurea or who could not tolerate a combination of metformin and a sulfonylurea	1 July 2020
Dulaglutide listed in combination with insulin and metformin unless metformin is contraindicated or not tolerated	1 March 2021
Semaglutide listed in combination with insulin and metformin unless metformin is contraindicated or not tolerated	1 September 2021
Exenatide delisted	1 February 2023

Current PBS listing details are available from the PBS website.

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

Dulaglutide

November 2017

The PBAC recommended the listing of dulaglutide for the treatment of T2DM in dual therapy in combination with metformin and in triple therapy in combination with metformin and a sulfonylurea at its November 2017 meeting, on the basis that it would be acceptably cost-effective if it were cost minimised against the once weekly and twice daily forms of exenatide (5 mcg + 10 mcg).

The submission applied a market share approach to estimate the use and financial implications of the requested listing on the PBS. The submission estimated dulaglutide would substitute for exenatide once weekly and exenatide twice daily (both strengths) at the same rates.

The commentary and the PBAC considered these substitution rates may be underestimated, particularly in the earlier years, as the dulaglutide once weekly presentation is easier to use than the exenatide once weekly presentation and it was likely that more patients would switch exenatide twice daily to dulaglutide once weekly.

The PBAC considered that the overall market for GLP-1 inhibitors may grow as a result of this listing with the potential for some substitution for insulin glargine.

For further details refer to the Public Summary Document from the November 2017 PBAC meeting.

July 2020

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 under the requested restriction would be acceptable if it were cost-minimised against exenatide 10 mcg twice daily.

For further details refer to the Public Summary Document from the July 2020 PBAC meeting.

May 2022

The PBAC recommended the listing of dulaglutide 3.0 mg and 4.5 mg for the treatment of T2DM in combination with metformin in patients who are contraindicated or intolerant to a combination of metformin and a sulfonylurea. The PBAC's recommendation for listing was based on, among other matters, its assessment, that the cost-effectiveness of dulaglutide 3.0 mg and 4.5 mg would be acceptable if it were cost-minimised against dulaglutide 1.5 mg.

For further details refer to the Public Summary Document from the March 2022 and May 2022 PBAC meetings.

October 2022 (Out of session)

The PBAC recommended the temporary listing of the s19A product dulaglutide 1.5 mg/0.5 mL solution for injection prefilled pen (Netherlands), TRULICITY on the PBS at the same ex-manufacturer price (effective price) as the PBS-listed dulaglutide which were in shortage.

The PBAC considered that there was a clinical need to maintain supply of dulaglutide on the PBS. The PBAC considered that the temporary listing should apply for the duration of the subsection 19A(1) approval.

For further details refer to the Public Summary Document from the October 2022 Out of session PBAC meeting.

Semaglutide

November 2019

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.

The PBAC's recommendation for listing was based on, among other matters, its assessment, as described above, that the cost-effectiveness of semaglutide would be acceptable if it were cost-minimised against dulaglutide.

The submission used a market share approach to estimate the utilisation and financial impact of listing semaglutide on the PBS/RPBS as part of dual/triple therapy for T2DM.

For further details refer to the Public Summary Document from the November 2019 PBAC meeting.

March 2020

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.

For further details refer to the Public Summary Document from the March 2020 PBAC meeting.

March 2021

The PBAC recommended extending the existing listing of semaglutide 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 semaglutide (both 0.5 mg once weekly and 1.0 mg once weekly) under the requested restriction would be acceptable if it was cost-minimised against dulaglutide 1.5 mg once weekly.

For further details refer to the Public Summary Document from the March 2021 PBAC meeting.

August 2022 (Out of session)

The PBAC recommended the temporary listing of the s19A products Ozempic 0.25 mg solution for injection in pre-filled pen (UK) and Ozempic 1 mg solution for injection pre-filled pen (UK) on the PBS at the same ex-manufacturer price as the two forms of PBS-listed semaglutide which were in shortage.

The PBAC considered that there was a clinical need to maintain the supply of semaglutide on the PBS. The PBAC considered that the temporary listing should apply for the duration of the subsection 19A(1) approval.

The PBAC noted reports that the increase in consumer demand for semaglutide has been driven by off-label prescribing for obesity management and this has resulted in the current shortages.

For further details refer to the Public Summary Document from the August 2022 PBAC meeting.

GLP-1 analogues

July 2023

The PBAC recommended the removal of the requirement for contraindication or intolerance to metformin for patients to use dipeptidyl peptidase 4 (DPP4) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors and GLP-1s in dual therapy with insulin. The PBAC recommended alignment of the PBS restrictions for DPP4 inhibitors, no longer restricting the use of some of these medicines in combination with insulin or SGLT2 inhibitors.

The PBAC recommended that the Authority Type for GLP-1 RAs, for therapy initiation for all indications, be changed from Authority Required (STREAMLINED) to Authority Required (Telephone/Online), but that continuing access should be via a streamlined authority. The PBAC further recommended that the use of GLP-1s in all T2DM indications should be restricted to patients who are contraindicated or intolerant to an SGLT2 inhibitor, or who do not achieve a clinically meaningful glycaemic response with an SGLT2 inhibitor. The PBAC considered that it may be appropriate to expand the PBS listings for GLP-1s to include use in combination with metformin, a sulfonylurea or insulin, for T2DM patients with a body mass index (BMI) greater than 35 kg/m2, without a requirement to trial an SGLT2 inhibitor. The PBAC requested that the Department provide financial estimates for this expanded listing to be considered at a future meeting.

For further details refer to the PBAC Web Outcomes from the July 2023 PBAC meeting.

Previous reviews by the DUSC

DUSC reviewed medicines for the treatment of T2DM at its October 2012, February 2013, February 2017 and September 2022 meetings.

The 2022 review included analyses of:

- Use of metformin, SU or insulin prior to GLP-1 RA initiation.
- Use of GLP-1 RAs in combination with another GLP-1 RA, an SGLT2 inhibitor or a DPP4 inhibitor.
- Use of a GLP-1 RA, SGLT2 inhibitor or a DPP4 inhibitor without concomitant use of metformin, a SU or insulin.

- It reported that there were several examples of apparent use outside the PBS restrictions:
    - From 2017 to mid-2022, 18% of people initiating GLP-1 RA therapy were not supplied metformin, a SU or insulin prior to or at initiation, indicating clear use outside of the PBS restrictions. A further 57% were supplied only insulin, a SU, or metformin prior to or at initiation of a GLP-1 RA, indicating possible use outside of the PBS restrictions.
    - According to analysis of the prevalent population in 2021, almost 60% of people supplied a GLP-1 RA received this medicine in a regimen that is inconsistent with the PBS restrictions:
        - 42% were supplied a GLP-1 RA in combination with another GLP-1 RA, a DPP4 inhibitor, an SGLT2 inhibitor or a combination of these medicines.
        - 27% were supplied a GLP-1 RA without concomitant use of metformin, SU or insulin.
        - 9.5% crossed both above categories and were supplied a GLP-1 RA without concomitant use of metformin, SU or insulin and in combination with another GLP-1 RA, a DPP4 inhibitor, an SGLT2 inhibitor, or a combination of these medicines.

For details of the DUSC consideration of diabetes medicines refer to the Public Release Documents.

Methods

Data extracted from the PBS claims database maintained by the Department of Health and Aged Care and processed by Services Australia were used for the analyses. Prescription data were extracted from 1 January 2016 up to and including 31 December 2023. Patients who were only supplied insulin in this period were excluded as they were likely to be patients with type 1 diabetes.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Services Australia Medicare date of processing data.[7] The publicly available Services Australia Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included. The Services Australia Medicare data used in this report includes under co-payment prescriptions from 1 April 2012.

Analysis of overall use of the diabetes market excluded prescriptions of flozins for kidney and cardiac PBS item codes.

Analysis of sequence of use for GLP-1 patients and initiating patients to flozins and gliptins before and after supply of GLP-1s used prescriptions of all diabetes medicines in the two years (730 days) prior to the patient initiating either semaglutide or dulaglutide. These analyses included prescriptions of flozins for kidney and cardiac PBS item codes.

The 2022 DUSC Analysis of T2DM medicines analysed combination treatment of a GLP-1 with flozins or gliptins. Combination treatment was defined as receiving a supply of one drug, drug A (e.g. GLP 1), with supply of another drug within 30 days, drug B (e.g. an alternative GLP 1, flozin or gliptin), and then a supply of drug A again within a subsequent 30 days (e.g. a GLP-1). Same day supply of a GLP-1 with another GLP-1, a flozin or a gliptin was also considered combination use.

The 2022 DUSC Analysis of T2DM medicines counted the number of supplies of GLP-1, flozins or gliptins in a row, without supplies of metformin, SU or insulin, for each patient. Patients with three or more supplies of a GLP-1, SGLT2 inhibitor or DPP4 inhibitor in a row following initiation, or a supply of metformin or SU, and patients with five or more supplies of a GLP-1, SGLT2 inhibitor or DPP4 inhibitor in a row following a supply of insulin were considered to be using the GLP-1, SGLT2 inhibitor or DPP4 inhibitor without concomitant therapy. The results from 2021 are represented and compared to the results from 2023.

Treatment duration was analysed using the Kaplan-Meier method. A patient was censored if they were supplied a prescription within three times the median time to resupply (29 days) prior to 31 December 2023 (i.e. 3×29 days).

Results

Analysis of drug utilisation

Overall utilisation

In 2023 there were approximately 1.6 million patients supplied one or more medicines through the PBS for T2DM, and 326,504 patients who were supplied a GLP-1.

[7] PBS statistics. Australian Government Services Australia. Canberra. Available from ,<http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>.

Table 4: Number of prevalent treated patients supplied T2DM medicines and GLP-1s by year

Year	Number of patients supplied one of more medicines for T2DM	Number of patients supplied a GLP-1	Number of patients supplied semaglutide or dulaglutide	Number of initiators to semaglutide or dulaglutide
2017	1,161,228	50,444		
2018	1,217,392	60,491	14,203	14,203
2019	1,265,758	75,489	40,198	27,815
2020	1,341,366	98,526	70,783	37,657
2021	1,426,753	172,055	162,340	98,813
2022	1,516,787	252,772	248,068	103,633
2023	1,604,963	326,504	325,993	120,374

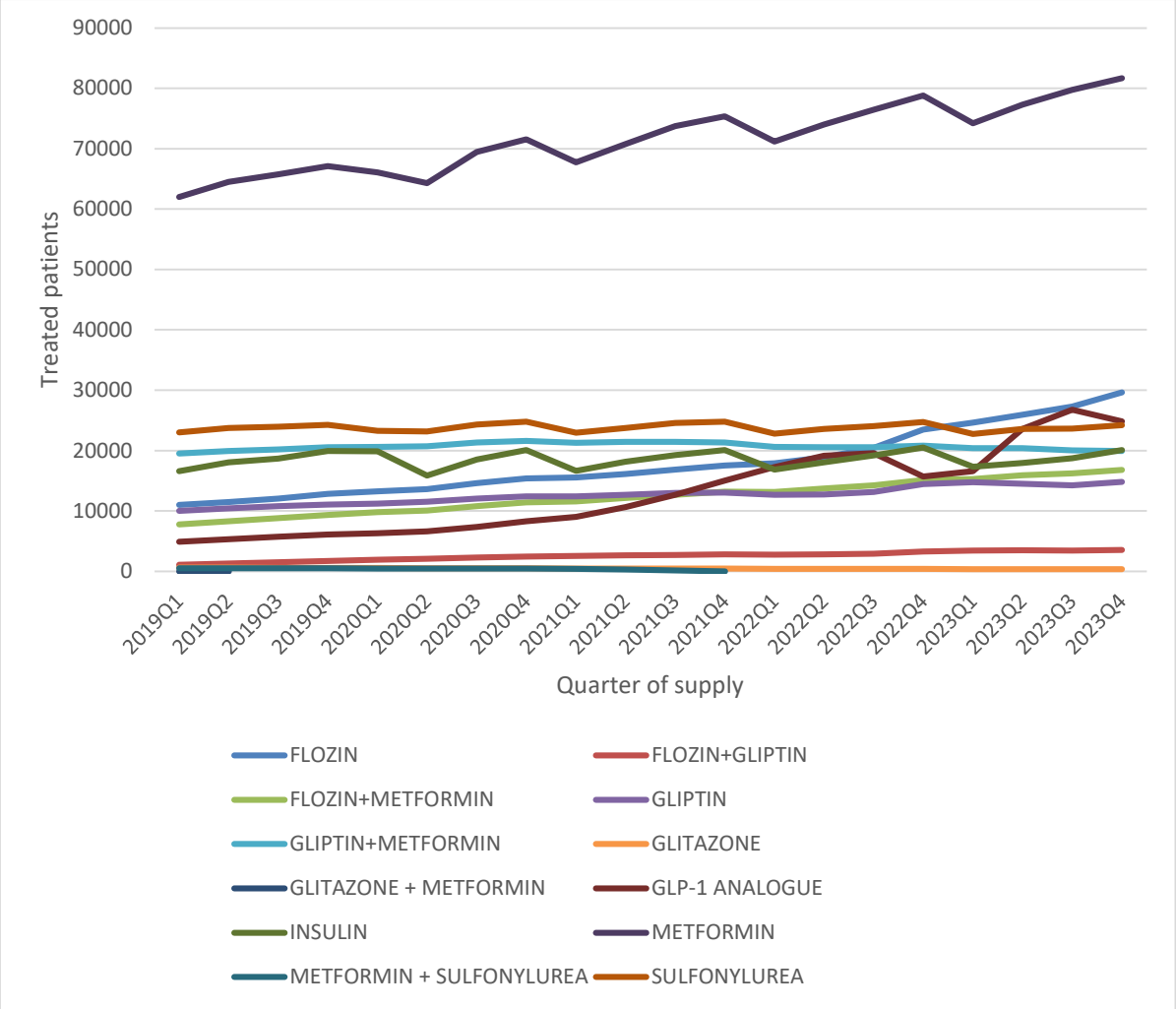

Figure 1: Number of patients supplied of T2DM medicines by class, including combinations

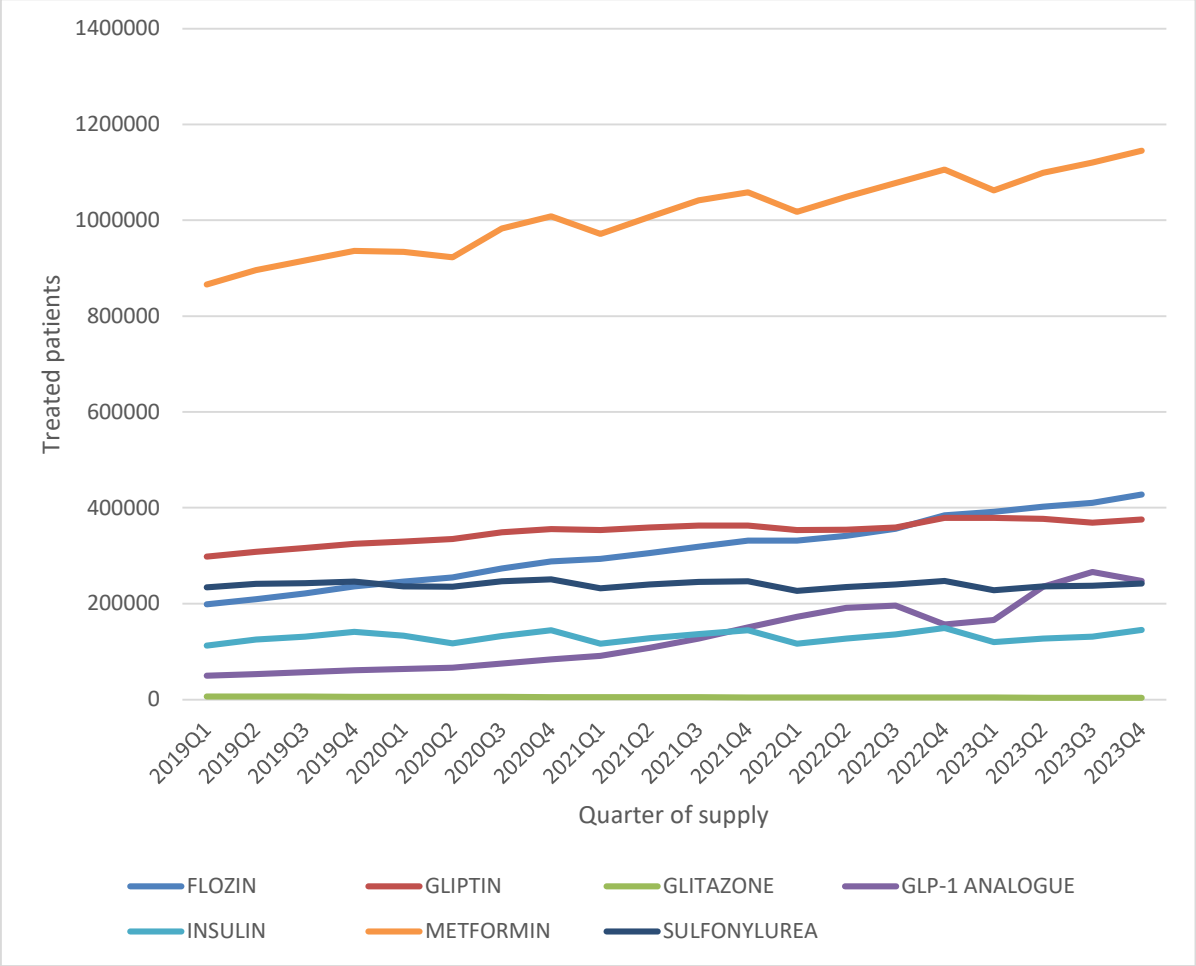

Figure 2: Overall use by singular class

Note: A patient supplied a combination medicine is counted in both classes

Metformin, including metformin as part of a combination supply, was supplied to the most patients, it was supplied to more than one million patients per quarter in 2023. The number of patients supplied GLP-1s appeared to be increasing beyond the number of patients supplied a sulfonylurea, however the GLP medicine shortage may have slowed this increase. Glitazones were supplied to less than 5,000 patients per quarter in 2023.

Utilisation of GLP-1s

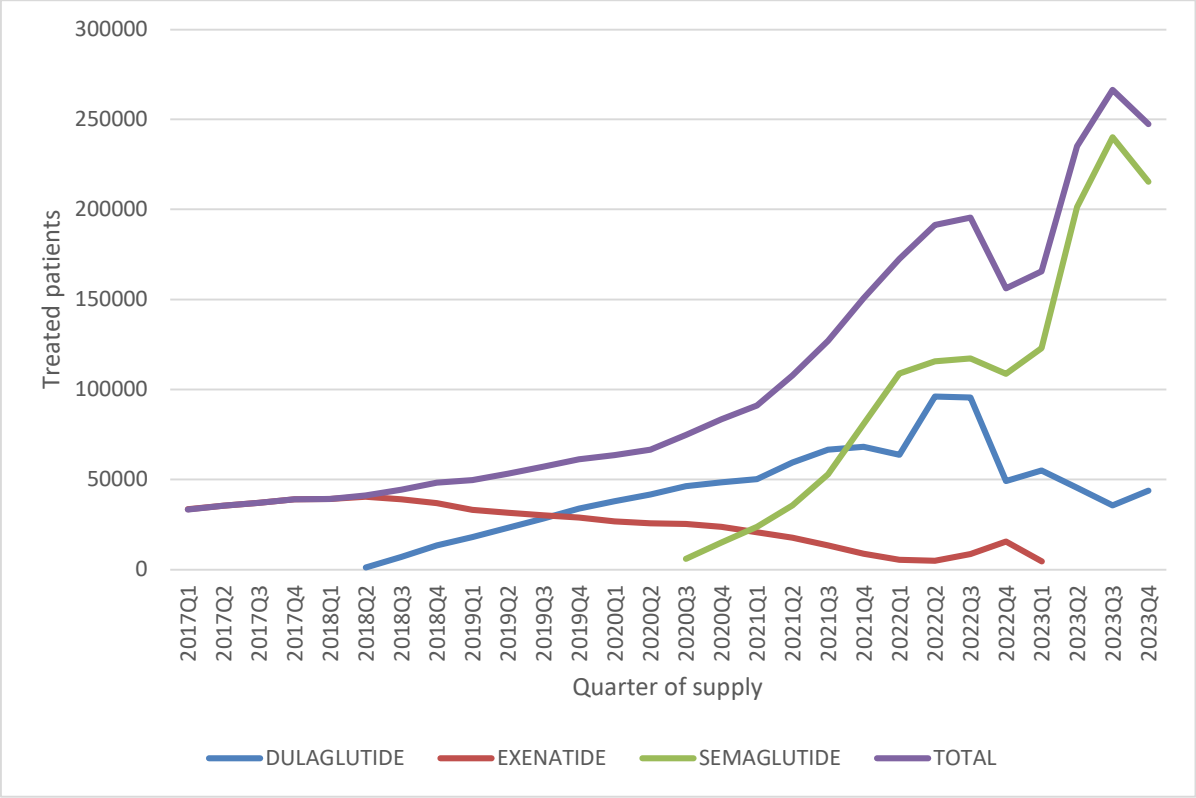

Figure 3: Patients supplied GLP-1s by medicine

Figure 3 shows that the use of semaglutide and dulaglutide increased when first listed on the PBS, with the use of exenatide decreasing from 2018, when dulaglutide was PBS listed, until exenatide was delisted from the PBS in 2023. The listing of semaglutide appeared to have taken some market share from dulaglutide, however the overall the total market had increased. The impact of the medicines shortage of semaglutide and dulaglutide can be seen in 2022, when the number of patients supplied each medicine first appeared to stabilise and then decreased. The temporary listing of s19A products may have reduced the number of affected patients, however it is possible that use would have been higher if dulaglutide and semaglutide had not been subject to the shortage.

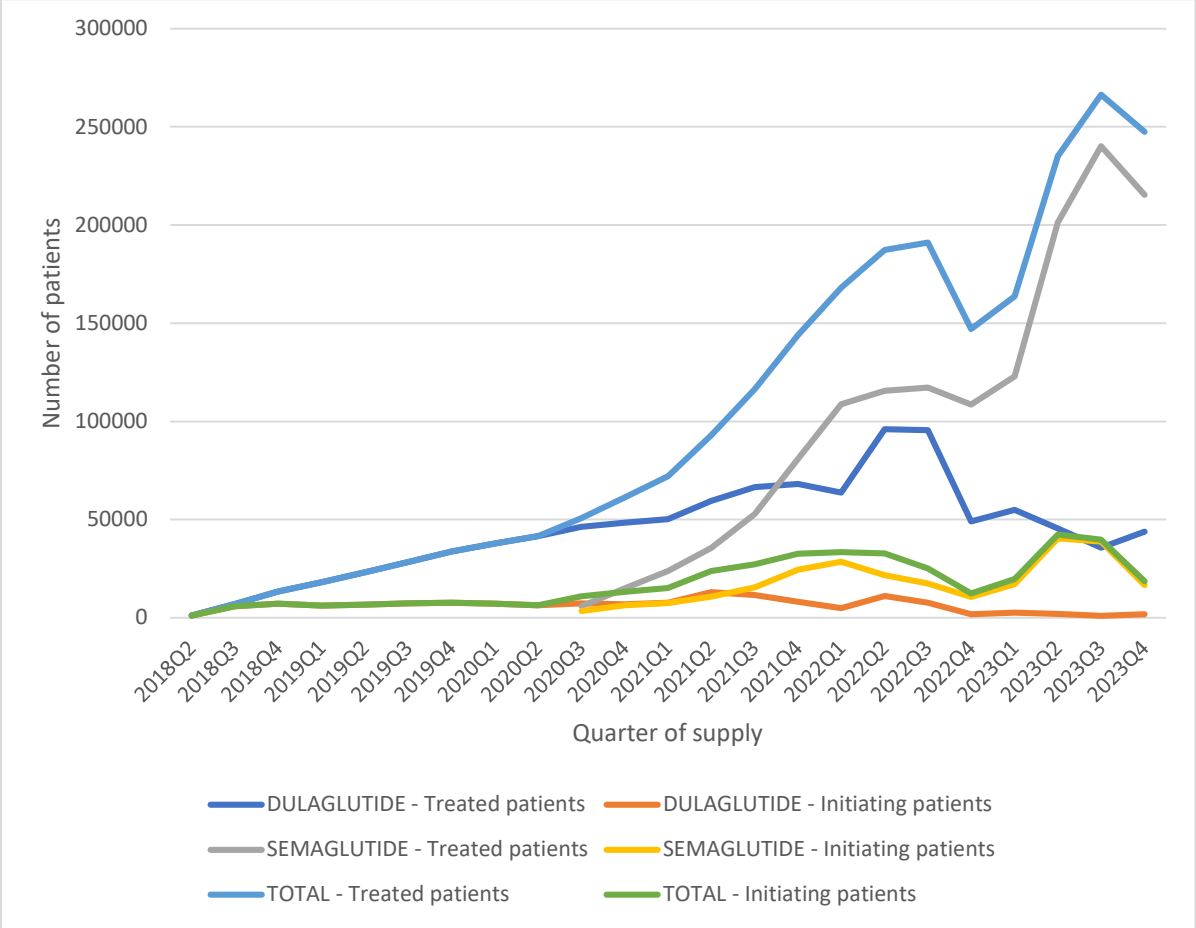

Figure 4: Number of initiating and treated patients for semaglutide and dulaglutide

Figure 4 shows the number of initiating and treated patients for semaglutide and dulaglutide, in which initiating patients were counted once for the first of the two medicines they were supplied. In 2023, 94% (113,058) of the patients who were supplied one of these medicines for the first time (120,374) were supplied semaglutide, compared to 6% (7,316) who were supplied dulaglutide.

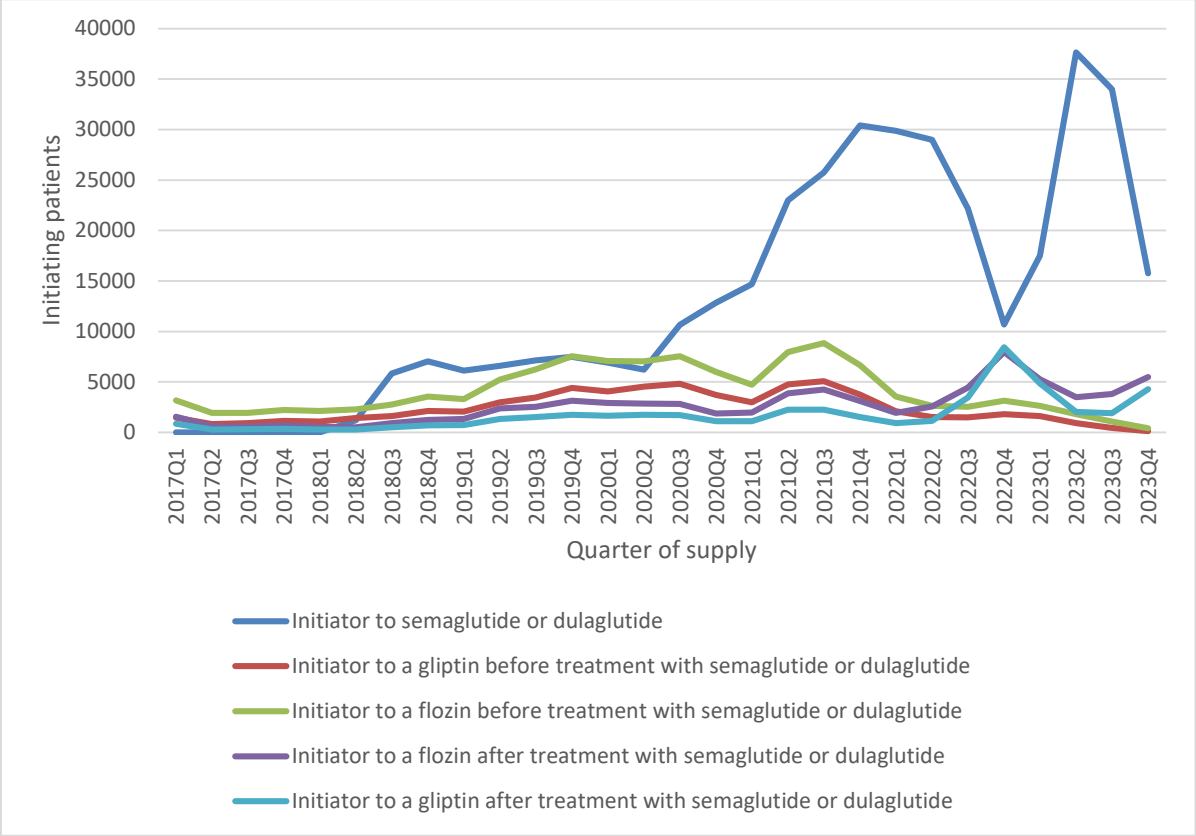

Figure 5: Initiating patients before and after treatment with semaglutide or dulaglutide

Figure 5 shows the number of patients initiating semaglutide or dulaglutide, and the number of patients who initiated a flozin or gliptin either before or after treatment with semaglutide or dulaglutide. A patient may be counted multiple times when they initiated semaglutide or dulaglutide, a flozin and a gliptin, but they were not counted twice as before and after treatment with semaglutide or dulaglutide. This figure shows that there was an increase in the number of patients who initiated flozins and gliptins after treatment with semaglutide or dulaglutide in 2022, which peaked in the fourth quarter of 2022. In the fourth quarter of 2022, 7,978 patients initiated a flozin and 8,459 patients initiated a gliptin following treatment with semaglutide or dulaglutide, compared to 3,092 patients who initiated a flozin and 1,515 patients who initiated a gliptin following treatment with semaglutide or dulaglutide in the fourth quarter of 2021. However, patients may be counted twice in a quarter if they trialled a flozin and gliptin in the same quarter. There were 16,077 patients who initiated a flozin or a gliptin after treatment with semaglutide or dulaglutide in the fourth quarter of 2022, compared with 4,574 patients in the fourth quarter of 2021. This suggests there may have been some patients previously treated with semaglutide or dulaglutide who initiated a flozin or gliptin due to the medicines shortage.

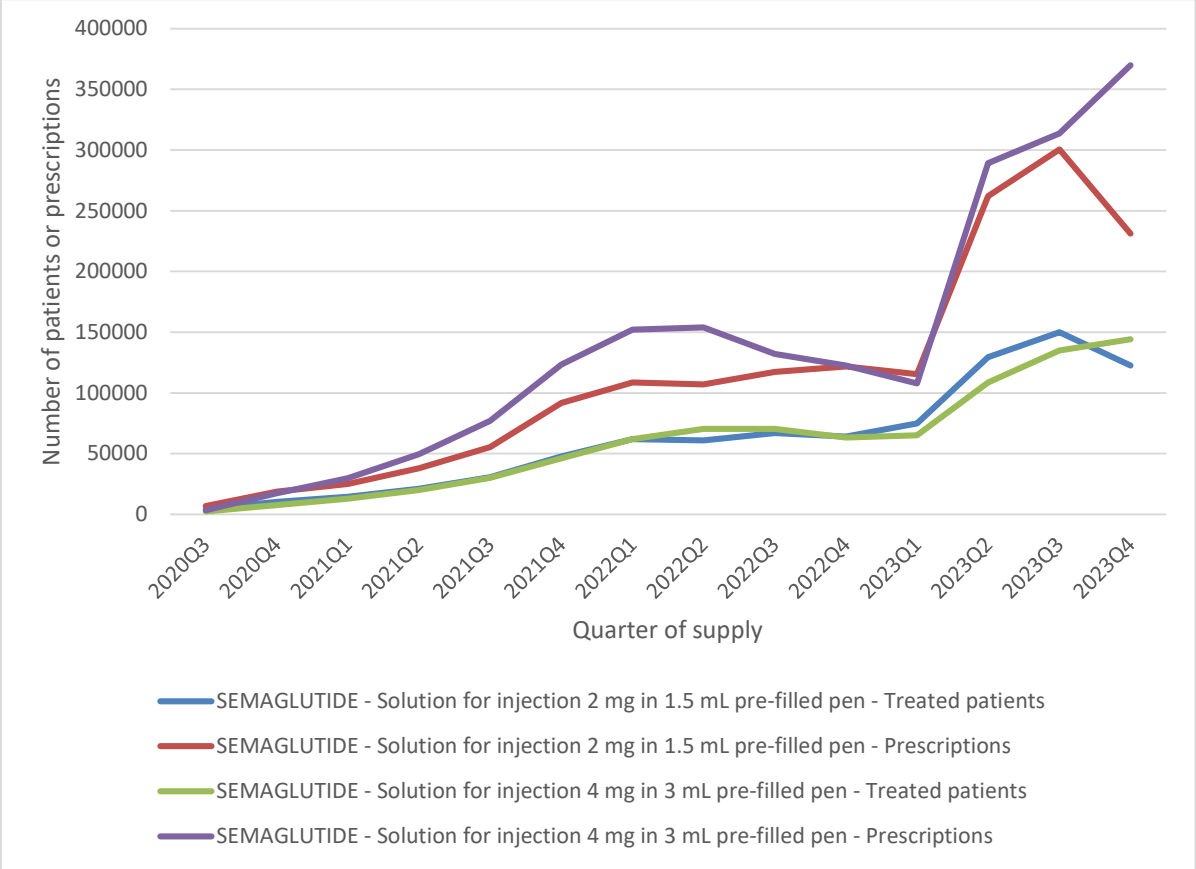

Figure 6: Number of patients and prescriptions of semaglutide by strength

Figure 6 shows that there was generally a higher supply of the higher dose, however this difference decreased between quarter 4 of 2022 and quarter 2 of 2023. The product information for semaglutide recommended a starting dose of 0.25 mg once weekly, which should be increased to 0.5 mg once weekly after 4 weeks. After at least 4 weeks with a dose of 0.5 mg once weekly, the dose can be increased to 1 mg once weekly to further improve glycaemic control. It is possible that during 2022 when the medicine shortage began, fewer patients were initiated to treatment, or patients were supplied lower doses of semaglutide. Figure 6 also shows that more distinct patients were supplied the lower dose during 2023, which may be due to new patients initiating on the lower dose.

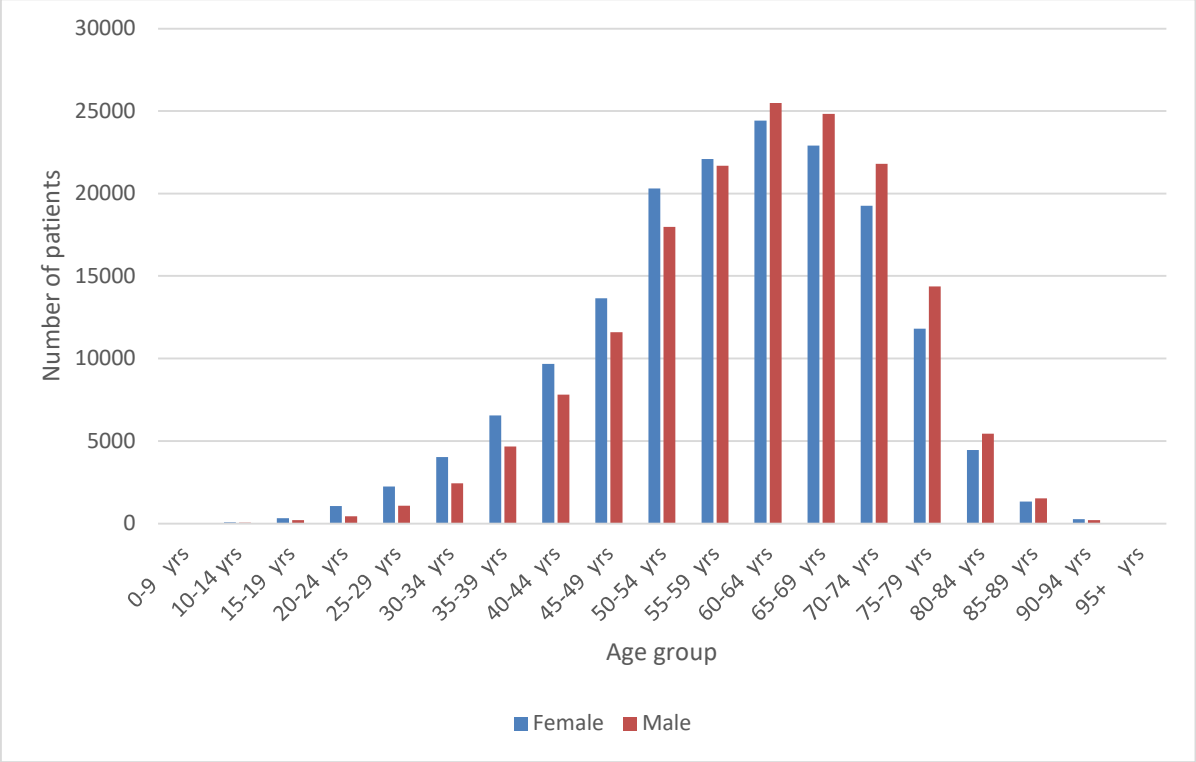

Figure 7: Age and gender of GLP-1 patients treated in 2023

Note: Using the age of the patient at the first supply in 2023, for semaglutide and dulaglutide only

Table 5: Mean and median age of GLP-1 patients treated in 2023

Gender	Number of patients	Mean	Median
Female	164,411	58.84	60
Male	161,582	60.98	62
Overall	325,993	59.90	61

Figure 7 suggests that there were proportionally more female patients younger than 60 years old treated in 2023, and proportionally more male patients 60 years and older treated in 2023. The mean and median ages of patients treated in 2023 confirms that the mean and median of female patients was approximately two years younger than those of male patients.

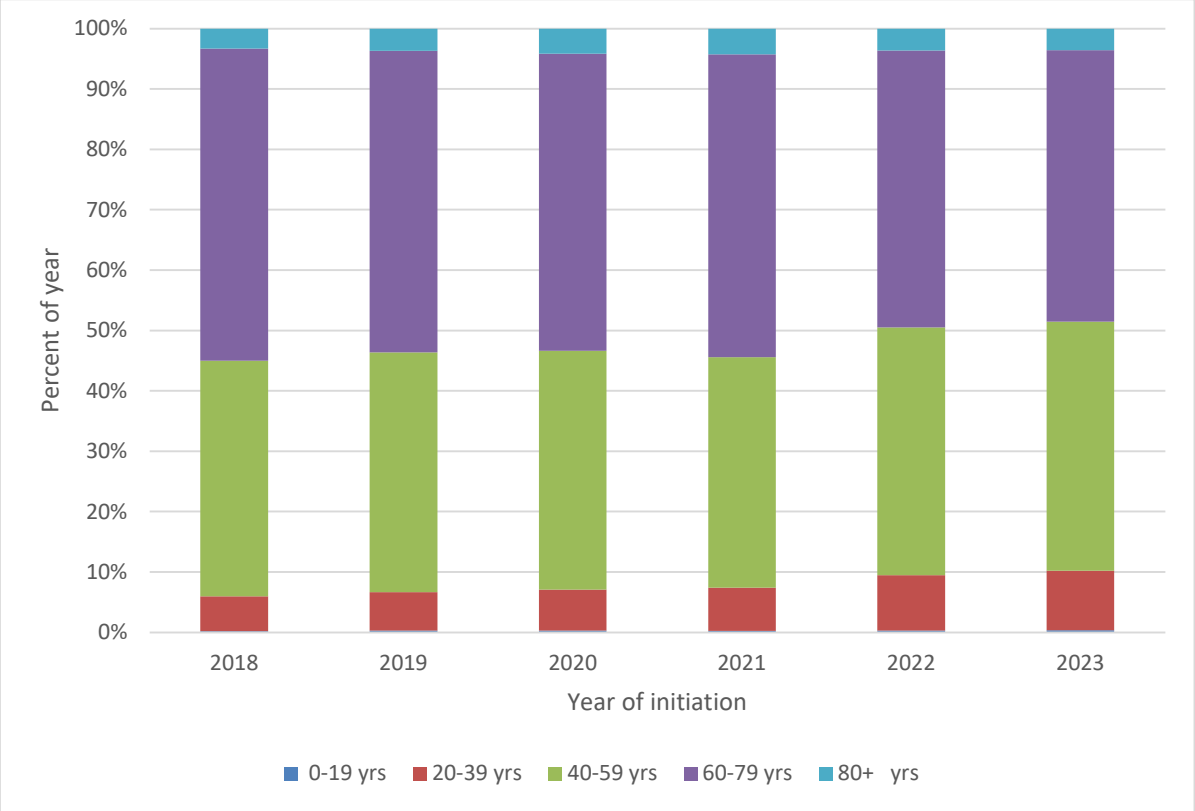

Figure 8: Age at initiation to semaglutide or dulaglutide by year of initiation

Table 6: Mean and median age of semaglutide and dulaglutide patients at initiation by year of initiation

Year	Number of patients	Mean	Median
2018	14,199	59.95	61
2019	27,809	59.66	61
2020	37,652	59.56	61
2021	98,813	59.82	61
2022	103,633	58.29	59
2023	120,374	57.91	59

Figure 8 and Table 6 show the age of patients at initiation to semaglutide and dulaglutide. It appeared there may be more younger patients initiating these medicines as the mean age decreased in every year except 2021. The percentage of patients in the 20-39 year old group has almost doubled from 2018, with 5.8% of patients aged 20-39 years old in 2018 and 9.8% of patients aged 20-39 years old in 2023.

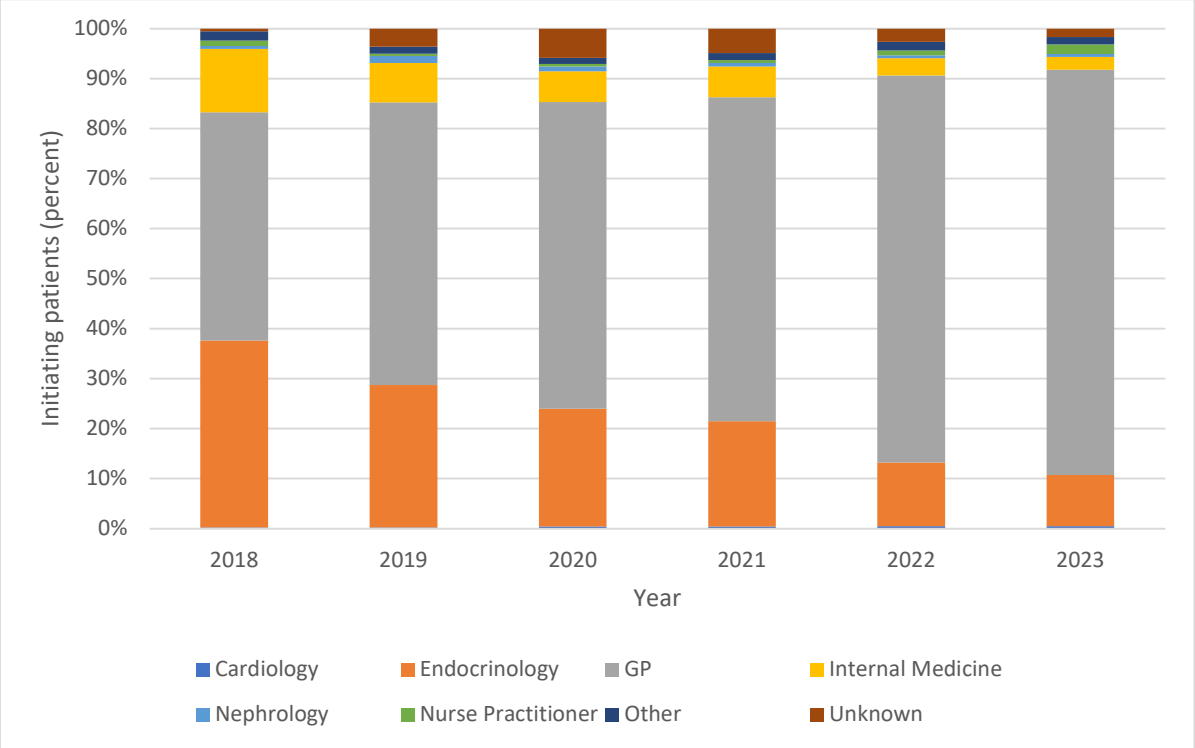

Figure 9: Prescriber type for initiating prescriptions of semaglutide and dulaglutide over time

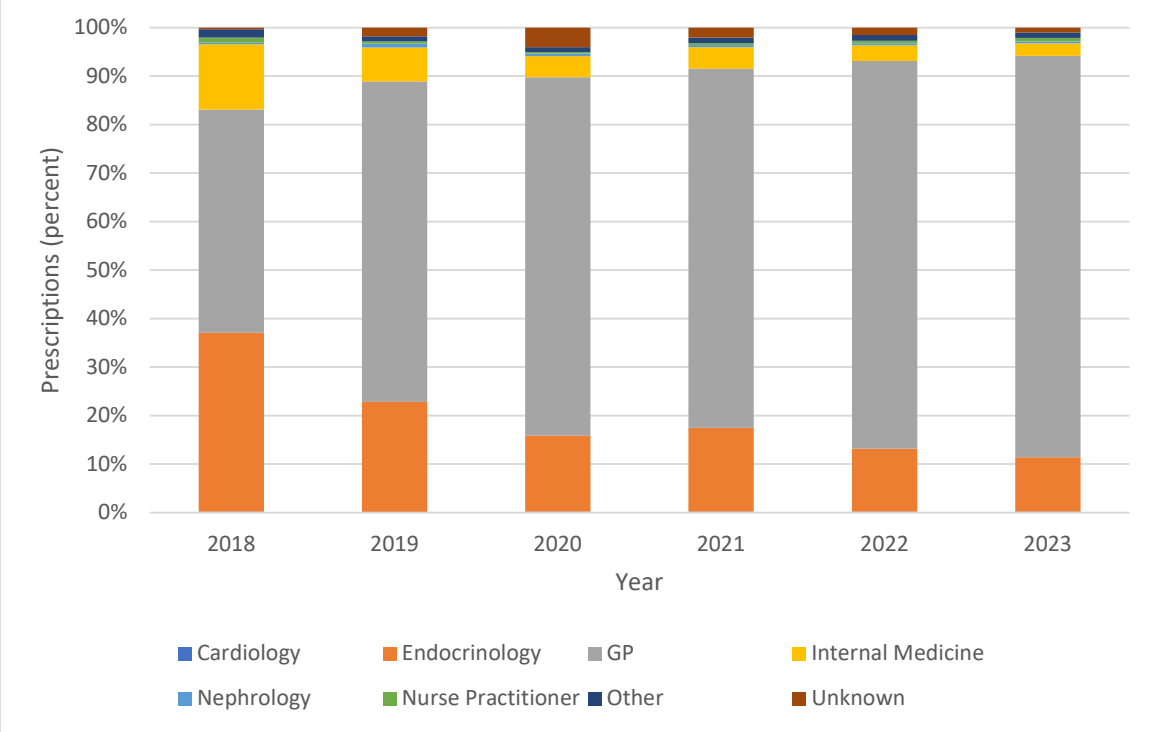

Figure 10: Prescriber type for all prescriptions of semaglutide and dulaglutide over time

It appeared that GP prescribing of semaglutide and dulaglutide to initiating patients and overall prescriptions for all treated patients had increased and prescribing by specialists had decreased. This was not restricted under the PBS restriction, however the reason for this increase was unclear.

Use of GLP-1s outside PBS restrictions

Table 7 summarises the medicine sequence of use by whether the patient was supplied semaglutide or any other medicine (including dulaglutide and flozins listed for non-diabetes indications) first. It appeared the proportion of patients who were supplied semaglutide before any other diabetes medicine was increasing, with 12% of initiating patients in 2023 supplied semaglutide before any other diabetes medicine.

Table 7: Number and proportion of GLP-1 patients supplied semaglutide first

	First supplied medicine			
Year	OTHER	SEMAGLUTIDE		TOTAL
		Number	Percent of total	
2018	14,203		0%	14,203
2019	27,815		0%	27,815
2020	37,381	276	1%	37,657
2021	94,740	4,073	4%	98,813
2022	93,303	10,330	10%	103,633
2023	105,542	14,832	12%	120,374

Note: Using a 2 year look back from initiation of semaglutide or dulaglutide, same day supplies were sorted with semaglutide last

Table 8: Analysis of the prevalent treated population

	2021	2023
Supplied a GLP-1 RA in combination with another GLP 1 RA, a DPP4 inhibitor, an SGLT2 inhibitor or a combination of these medicines	42%	44%
Supplied a GLP-1 RA without concomitant use of metformin, SU or insulin	27%	42%
Crossed both above categories and were supplied a GLP-1 RA without concomitant use of metformin, SU or insulin and in combination with another GLP 1 RA, a DPP4 inhibitor, an SGLT2 inhibitor, or a combination of these medicines	9.5%	15.9%
Proportion of patients supplied GLP-1 who received this medicine in a regimen that is inconsistent with the PBS restrictions	60%	70%

The comparison of 2021 to 2023 suggests the number of patients using GLP-1s outside PBS restrictions may have been increasing. The TGA reported that demand for semaglutide had accelerated in 2023, particularly for the low-dose (0.25/0.5 mg) product. This additional

demand was caused mainly by a rapid increase in prescribing for 'off-label' use (prescriptions to treat conditions other than those approved by the TGA).[8, 9]

Length of treatment

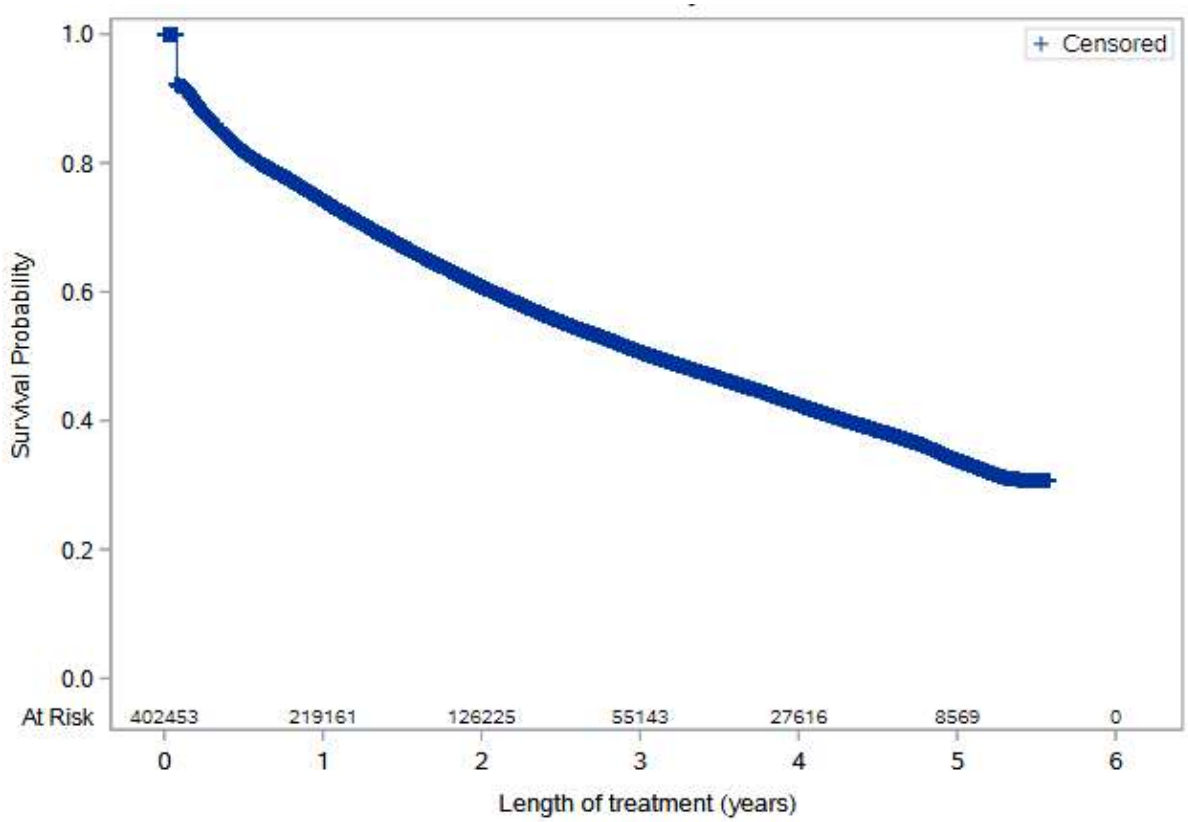

Figure 11: Length of treatment for semaglutide and dulaglutide

Of 402,453 patients included in the analysis, 61% (246,524) were considered to be continuing treatment at the end 2023 and were censored. The length of treatment was estimated to have a mean and median of 3 years, however it was noted that the mean length of treatment and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

[8] The Department of Health and Aged Care, Therapeutic Goods Administration, Information about major medicine shortages, accessed 2 May 2024, updated 21 September 2023. Available from: https://www.tga.gov.au/safety/shortages/information-about-major-medicine-shortages/about-ozempic-semaglutide-shortage-2022-and-2023

[9] Day RO. Ongoing challenges of off-label prescribing. Aust Prescr 2023;46:86-9. https://doi.org/10.18773/austprescr.2023.022

Table 9: Quartile Estimates from Kaplan Meier analysis

Percent	Point Estimate	Transform	95% Confidence Interval	
			Lower	Upper
75		LOGLOG	.	.
50	3.07	LOGLOG	3.05	3.10
25	0.95	LOGLOG	0.93	0.95

Table 10: Estimated mean from Kaplan Meier analysis

Mean	Standard Error
3.04	0.004

Note: The mean length of treatment and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

Discussion

Despite the medicines shortages of semaglutide and dulaglutide, the use of GLP-1s within the T2DM market was increasing and the number of supplied prescriptions and patients treated with these medicines had increased beyond the previous use of exenatide. Semaglutide was the most used GLP-1, accounting for 83% of the prescriptions supplied in 2023.

Semaglutide and dulaglutide were both recommended on a cost minimisation basis, although in its first recommendation of dulaglutide the PBAC did consider that the overall market for GLP-1 inhibitors may grow as a result of the PBS listing of dulaglutide.

It appeared that GP prescribing of semaglutide and dulaglutide had increased and prescribing by specialists had decreased over the last six years. In 2018, 46% of patients initiated to dulaglutide were initiated by GPs and 50% of patients were initiated by Endocrinology or Internal Medicine specialists. Of the patients who initiated semaglutide or dulaglutide in 2023, 81% were initiated by GPs and 13% of patients were initiated by Endocrinology or Internal Medicine specialists. The PBS restrictions for semaglutide and dulaglutide do not limit prescribing to specialists, however the reason for this increase is unclear.

It appears there may be more younger patients initiating these medicines as the mean age decreased in every year except 2021. The percentage of patients in the 20-39 year old group had almost doubled from 2018, with 5.8% of patients aged 20-39 years old in 2018 and 9.8% of patients aged 20-39 years old in 2023. This may be due to a combination of factors such as younger patients being diagnosed with T2DM, and younger people being exposed to information regarding weight loss due to semaglutide through social media.[8,9]

The shortage of semaglutide and dulaglutide, which was first reported in 2022, appeared to have impacted use, by reducing the number of initiating and treated patients, and causing an increase in the number of patients initiating flozins and gliptins following supplies of GLP-1s.

It appeared that there had likely been use of GLP-1s outside the PBS restrictions, as 12% of patients who initiated semaglutide in 2023 had no prior supplies of any other diabetes medicine, including metformin and insulin, and 42% of patients supplied a GLP-1 in 2023 were not supplied concomitant use of metformin, SU or insulin. This may indicate that there were patients supplied a GLP-1 through the PBS for a reason other than diabetes management.

In July 2023, the PBAC recommended that the Authority type for GLP-1s, for therapy initiation for all indications, be changed from Authority Required (STREAMLINED) to Authority Required (Telephone/Online), but that continuing access should be via a streamlined authority. These changes had not yet been implemented and may help to ensure GLP1-s are used to treat T2DM patients who require improved glycaemic control.

DUSC consideration

DUSC noted that the number of supplied prescriptions of GLP-1s had increased over time, despite a temporary decrease in the fourth quarter of 2022 and the first quarter of 2023. DUSC noted that there were more prescriptions of GLP-1s than of sulfonylurea supplied in the third quarter of 2023, that the use of semaglutide and dulaglutide had increased beyond the projected use of exenatide, and that semaglutide has a high proportion of the market share.

The report showed that there were 16,077 patients who initiated a flozin or a gliptin after treatment with semaglutide or dulaglutide in the fourth quarter of 2022, compared with 4,574 patients in the fourth quarter of 2021. DUSC agreed that it appeared there were patients previously treated with semaglutide or dulaglutide who initiated a flozin or gliptin due to the medicines shortage.

The report showed that there were proportionally more female patients younger than 60 years old treated in 2023, and proportionally more male patients 60 years and older treated in 2023. The percentage of patients in the 20-39 year old group almost doubled from 2018, with 5.8% of patients aged 20-39 years old in 2018 and 9.8% of patients aged 20-39 years old in 2023.

The response from Eli Lilly Australia Pty Ltd, the sponsor of dulaglutide, noted, “Globally, there is a growing body of evidence highlighting a substantial increase in the prevalence of T2DM in patients aged <40 years, also referred to as young-onset T2DM (Sadat, 2023; Xie et al., 2022). Furthermore, patients with young-onset T2DM experience a greater disease burden and higher lifetime risk of developing T2DM-associated complications than patients diagnosed with T2DM at later stages in life (Magliano et al., 2020).” DUSC disagreed with the sponsor and noted that the published epidemiology suggests the prevalence in patients under the age of 40 is much lower than PBS use.[10] DUSC commented that social media had

[10] Australian Institute of Health and Welfare. Diabetes: Australian facts [Internet]. Canberra: Australian Institute of Health and Welfare, 2024 [cited 2024 Jun. 28]. Available from: https://www.aihw.gov.au/reports/diabetes/diabetes

a strong impact on the use of GLP-1 medicines in young people, and suggested patients in the 20-39 age range may try to access semaglutide to treat diabetes and for weight loss, and for other reasons such as fertility.

GP prescribing of semaglutide and dulaglutide to initiating patients and overall prescriptions for all treated patients had increased and prescribing by specialists had decreased. DUSC noted that the PBS restriction did not limit GP prescribing of GLP-1s but suggested that as prescribing from endocrinologists had not increased in line with the use of GLP-1s, the increase in the supply of GLP-1s may not be for patients with complex diabetes.

DUSC noted that the proportion of patients who were supplied semaglutide before any other diabetes medicine had increased, with 13% of initiating patients in 2023 supplied semaglutide before any other diabetes medicine. DUSC noted that the demand for semaglutide had accelerated in 2023, particularly for the low-dose (0.25/0.5 mg) product, and considered this was likely due to an increase in prescribing for 'off-label' use.

DUSC considered that the supply of semaglutide to diabetic patients outside of the PBS restrictions was a lesser concern than non-diabetic patients being supplied semaglutide through the PBS. DUSC commented that it had not been shown to be cost-effective for these patients, and it may mean that eligible patients were not able to access treatment.

DUSC commented that the prevalence of diabetes had been reported as approximately 40% in central Australia[11], and considered there may be a demand for this medicine among the Aboriginal and Torres Strait Islander population which cannot be met due to shortages and use outside the restriction.

DUSC noted that the response from Eli Lilly Australia considered there were issues with the methods used, in particular that:

- Analysis of PBS dispensing data provides insights into the medicines a patient has been supplied; it does not consider the medications prescribed to a patient by a health care provider or the medicines a patient consumes.
- Failure to consider overlap in the supplies of medicines when patients switch from one line of therapy to the next is likely to overestimate the use of GLP-1 RAs in combination with DPP4 inhibitors and SGLT2 inhibitors.
- The use of median standard coverage days to determine co-medication thresholds is likely to underestimate GLP-1 RA co-medication with metformin, sulfonylureas, and insulin as there is considerable variation in the time between purchases for patients utilising these medicines. Misclassification of GLP-1 RA supply without concomitant metformin, sulfonylurea or insulin is likely further exacerbated as there is a failure

[11] Hare MJL, Zhao Y, Guthridge S, Burgess P, Barr ELM, Ellis E, Butler D, Rosser A, Falhammar H, Maple-Brown LJ. Prevalence and incidence of diabetes among Aboriginal people in remote communities of the Northern Territory, Australia: a retrospective, longitudinal data-linkage study. BMJ Open. 2022 May 15;12(5):e059716. doi: 10.1136/bmjopen-2021-059716. PMID: 35569825; PMCID: PMC9125760.

to account for dose modifications which can further extend the time between supplies of metformin, sulfonylureas, and insulin.

DUSC noted that different standard coverage days were used for different classes of medicine to determine co-prescribing. DUSC considered other factors described in the report, such as the number of patients supplied semaglutide before any other diabetes medicine, suggest that there had been use outside the PBS restriction.

DUSC commented that future analyses using linked PBS and MBS data could be considered to determine what proportion of patients had their HbA1C tested and were likely diabetic.

DUSC actions

DUSC requested that the report be provided to the PBAC for consideration.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Novo Nordisk Pharmaceuticals Pty. Limited: The sponsor had no comment.

Eli Lilly Australia Pty Ltd: The sponsor had no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to

define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health and Aged Care has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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