

## 10.04 DUSC analysis of medicines for the treatment of type 2 diabetes

### 1 Purpose of item

- 1.1. To consider advice from the Drug Utilisation Sub Committee (DUSC) on the utilisation of medicines for the treatment of type 2 diabetes mellitus (T2DM) with a focus on the use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs), sodium-glucose cotransporter 2 (SGLT2) inhibitors and dipeptidyl peptidase-4 (DPP4) inhibitors outside the Pharmaceutical Benefits Scheme (PBS) restrictions.

### 2 Background

The DUSC analysis of medicines for the treatment of T2DM (September 2022) found the following:

- 1.2. In 2021, the total number of people supplied a medicine for the treatment of T2DM through the PBS was around 1.42 million.
- 1.3. In mid-2022, biguanides (metformin) were the most commonly supplied class of medicines for the treatment of T2DM, followed by (in order), DPP4 inhibitor + metformin FDCs, SGLT2 inhibitors, GLP-1 RAs, and SUs.
- 1.4. Total annual expenditure based on the published list prices on T2DM medicines has increased from around \$516 million in 2017-2018 to around \$756 million in 2021-22.
- 1.5. GLP-1 RAs are now the highest expenditure class of medicines on the PBS for the treatment of T2DM accounting for 26% of expenditure in 2021-22 (\$194 million).
- 1.6. There are 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.
- 1.7. In 2021, around 15% of people supplied an SGLT2 inhibitor and 16% of people supplied a DPP4 inhibitor received these medicines without concomitant use of metformin, SU or insulin, as required by the PBS restrictions.
  - 1.8. In 2021, around 14% of people supplied an SGLT2 inhibitor and 7% of people supplied a DPP4 inhibitor received these medicines in combination with a GLP-1 RA, use which is inconsistent with the PBS restrictions.

### **3 PBAC Outcome**

- 1.9. The PBAC noted the increasing use and expenditure on T2DM medicines through the PBS during 2017-2022, particularly for GLP-1 RAs and SGLT2 inhibitors. The PBAC noted the decline in expenditure on insulin for the treatment of T2DM over this period.
- 1.10. The PBAC noted the substantial use of GLP-1 RAs outside of the PBS restrictions, including use as a first-line therapy, use without required concomitant therapies, and use in combination with DPP4 and SGLT2 inhibitors. The PBAC also noted that there was some use of SGLT2 and DPP4 inhibitors outside of the PBS restrictions, including likely use in monotherapy, as a first-line therapy, and use in combination with a GLP-1 RA. However, the PBAC considered that some of this use was likely to be in accordance with Australian and international clinical treatment guidelines and considered that there was growing misalignment between clinical guidelines and the PBS restrictions.
- 1.11. The PBAC considered that many clinicians may have a broader view of contraindication to sulfonylurea due to the association of this class with increased risk of hypoglycaemia and weight gain.
- 1.12. The PBAC noted that while metformin remains the most common medicine to initiate T2DM therapy, there was a rapid increase in the number of patients initiating T2DM therapy with a GLP-1 RA or SGLT2 inhibitor since 2021. The PBAC considered that it was still appropriate for patients without a contraindication to initiate first-line T2DM drug therapy with metformin prior to initiation of a GLP-1 RA, SGLT2 inhibitor or DPP4 inhibitor, and that most clinical guidelines supported this treatment pathway.
- 1.13. The PBAC considered that there may be some prescriber confusion regarding the restrictions (and clinical indications) for T2DM medicines, given evidence of sub-optimal prescribing, such as co-prescribing of DPP4 inhibitors and GLP-1 RAs.
- 1.14. The PBAC considered prescribing of GLP-1 RAs concomitantly with DPP4 inhibitors to be both clinically inappropriate and non-cost-effective, as there is currently no evidence to support the use of this combination. The PBAC also noted some use of GLP-1 RAs with SGLT2 inhibitors, which has not been considered by the PBAC for cost-effectiveness. The PBAC noted that the PBS restrictions for SGLT2 inhibitors and DPP4 inhibitors contain a 'Note' that these medicines are not subsidised for use in

combination with a GLP-1 RA. The PBAC considered that it may be useful to move this requirement to an exclusionary 'Treatment Criterion' to aid in drawing this requirement to the attention of prescribers. The PBAC advised that it may also be appropriate for the Department to consider quality use of medicines educational activities on this topic for prescribers, pharmacists, and consumers.

- 1.15. The PBAC requested that the Department draft restriction changes to amend the restriction type for GLP-1 RAs from Authority Required (STREAMLINED) for all indications to Authority Required (telephone/online). The PBAC further requested that the restrictions for dual therapy with metformin/sulfonylurea include a requirement that patients initiating treatment with a GLP-1 RA be contraindicated/intolerant to an SGLT2 inhibitor, but that the requirement for contraindication/intolerance to a combination of metformin and a sulfonylurea could be removed. In making this request, the PBAC noted the increasing use of GLP-1 RAs outside of the PBS restrictions and the high cost of these medicines compared to alternative treatments.
- 1.16. The PBAC recalled that both SGLT2 inhibitors and GLP-1 RAs were listed for dual therapy with metformin/sulfonylurea based on a series of non-inferiority comparisons originating from insulin, and that the subsequent price reduction for SGLT2 inhibitors in 2015 meant that SGLT2 inhibitors were likely to be more cost-effective than GLP-1 RAs when used in dual therapy with metformin or a sulfonylurea. The PBAC also considered that expanding access to semaglutide and dulaglutide would be impractical in the context of the current supply issues for these medicines.
- 1.17. The PBAC considered that it was appropriate that patients who had legitimately qualified for PBS-subsidised access under the previous restrictions for dual therapy with a GLP-1 RA and metformin/sulfonylurea should continue to have access to these medicines, without the requirement for contraindication/intolerance to an SGLT2 inhibitor.
- 1.18. The PBAC noted that dulaglutide is currently subsidised for dual therapy with metformin only, while semaglutide and exenatide are subsidised for use in combination with metformin or a sulfonylurea. The PBAC further noted that GLP-1 RAs are PBS-listed for triple therapy with metformin and a sulfonylurea. The PBAC considered that it would be appropriate to reduce the complexity of the restrictions for prescribers by aligning the restrictions and extending the listing of dulaglutide to include dual therapy with a sulfonylurea. The PBAC noted that this was within the listed indications for dulaglutide on the Australian Register of Therapeutic Goods (ARTG), and that the Product Information for both dulaglutide and semaglutide included a similar precaution regarding the risk of hypoglycaemia when used in combination with insulin or a sulfonylurea.<sup>12</sup> The PBAC considered that the cost-effectiveness of the use of dulaglutide in combination with a sulfonylurea, would be similar to that of semaglutide in combination with a sulfonylurea, and that the change would have a negligible impact on cost to the PBS.

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<sup>1</sup> ARTG, [Product Information: Ozempic® \(semaglutide\) solution for injection](#), accessed: 18/11/2022.

<sup>2</sup> ARTG, [Product Information: Trulicity \(dulaglutide RCH\) autoinjector](#), accessed: 18/11/2022.

- 1.19. The PBAC requested that the Department develop the draft restriction changes for GLP-1 RAs detailed above and provide costings for consideration at a future meeting.
- 1.20. The PBAC considered that changing the restriction type for GLP-1 RAs from the current Authority Required (STREAMLINED) to Authority Required (telephone/online) may have the unintended consequence of increasing SGLT2 inhibitor and DPP4 inhibitor use outside of the PBS restrictions, particularly use in monotherapy. The PBAC considered that it would be appropriate to review the utilisation of T2DM medicines in 12-24 months to monitor the effectiveness of the GLP-1 RA restriction changes and any unintended consequences.
- 1.21. The PBAC noted that in 2021 around 15% of patients supplied an SGLT2 inhibitor or DPP4 inhibitor, did not receive this medicine in combination with metformin, a sulfonylurea, or insulin as required by the PBS restrictions, and around 14% of people supplied an SGLT2 inhibitor and 7% of people supplied a DPP4 inhibitor received these medicines in combination with a GLP-1 RA. The PBAC considered that a price reduction of at least 15% in the cost of DPP4 inhibitors and SGLT2 inhibitors would be appropriate to account for the proportion of use outside the restrictions for which cost-effectiveness has not been considered.
- 1.22. The PBAC foreshadowed that in the absence of relevant sponsors accepting a price reduction, it is of a mind to recommend a change to the restriction type for SGLT2 inhibitors and DPP4 inhibitors from the current Authority Required (STREAMLINED) type to Authority Required (telephone/online) to reduce use outside the PBS restrictions.