

Type 2 diabetes: reducing the impact of cardiovascular and renal disease

Therapeutic Brief

Key Points

- **Early and continuing lifestyle interventions are the foundation of diabetes management.**

- **Metformin is the first line medicine in type 2 diabetes unless contraindicated or not tolerated.**

- **Consider early use of SGLT2 inhibitors for people with comorbidities.**

- **Be aware of recent changes in the PBS restrictions impacting access to the use of SGLT2 inhibitors and GLP-1A medicines.**

Diabetes is the fastest growing chronic condition in Australia, increasing at a faster rate than other chronic diseases such as heart disease and cancer.

Type 2 Diabetes Mellitus (T2DM) is increasingly diagnosed in younger adults, adolescents and even children.¹ Emerging evidence suggests that early-onset T2DM is a more aggressive disease than later-onset T2DM and is associated with more rapid progression of macrovascular and microvascular complications.¹ The most common cause of death in people living with diabetes is cardiovascular disease (CVD). ●



Does your patient have a high risk of CVD or CKD?

It is important to regularly assess the absolute cardiovascular risk and risk of chronic kidney disease (CKD) for all your patients with T2DM.



Risk of chronic kidney disease (CKD)
[CKD risk calculators](#)



[CKD risk calculators](#)



Cardiovascular risk
[Australian cardiovascular risk calculator](#)



[Australian cardiovascular risk calculator](#)

Ensure patients with established CVD or high absolute cardiovascular risk (>10%) are also on lipid lowering therapy and blood pressure lowering therapy. These medicines are underused in this high-risk population.²⁻⁴ ●

What actions to take and when?

Prevention is better than cure - public health interventions are important and beneficial. There is increasing evidence for, and interest in, the concept of 'diabetes remission' using intensive nutritional and lifestyle interventions early after diagnosis.⁴⁻⁶

Always reinforce the benefits of lifestyle intervention and the need for exercise and diet modification throughout the course of the disease.

Metformin

[Metformin](#) is the first-line medicine to use in treating patients with T2DM unless contraindicated or not tolerated.⁷ Metformin is mostly very well tolerated, provides effective HbA1c reduction, and improves cardiovascular outcomes.^{2, 5, 8} >



[Always reinforce the benefits - RACGP Handbook](#)



[Metformin PBS information](#)



The only other [PBS](#) subsidised options for monotherapy in type 2 diabetes are sulfonylureas (SU), acarbose, insulin, and pioglitazone. ●



PBS Benefits Scheme

Medicines with cardiovascular and renal benefits

Sodium-glucose co-transporter 2 (SGLT2) inhibitors and Glucagon-Like Peptide-1 Receptor Agonists (GLP-1As) have proven cardiovascular and renal benefits. They should be prioritised when adding to metformin and where possible should be started without delay in patients who have established cardiovascular or CKD or are at high risk of developing these complications.^{4, 7, 9-11}

These two classes of drugs also give protection against major CVD in those with established atherosclerotic cardiovascular disease (ASCVD).^{9, 12} In addition to their glucose lowering effects, SGLT2 inhibitors and GLP1-As also slow the progression of kidney disease.⁹

These cardiovascular and renal benefits are independent of their glycaemic lowering effects. ●

Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors

SGLT2 inhibitors (dapagliflozin and empagliflozin) are available as tablets. They work by inhibiting the sodium-glucose co-transporter 2, reducing glucose reabsorption in the kidney and increasing urinary glucose excretion.¹²

SGLT2 inhibitors rely on adequate glomerular filtration for their glycaemic benefit and are not as effective at glycaemic control in patients with CKD. However, they still should be considered in these patients for their renal benefit. Check renal function before starting treatment and then periodically as clinically indicated.¹³ You may see an initial decrease in eGFR but this should stabilise.¹⁴ >



Warning

The risk of developing euglycaemic ketoacidosis with SGLT2 inhibitors is increased in patients:

- with vomiting or diarrhoea
- fasting for a prolonged time
- who have a low carbohydrate diet
- with severe dehydration
- who have excessive alcohol intake
- in whom perioperative guidelines require fasting or reduced fluid intake.

SGLT2 inhibitors need to be withheld in these circumstances.

Glucagon-Like Peptide 1 Receptor Analogues (GLP1-As)

In Australia, only injectable forms of GLP-1As are available: dulaglutide, semaglutide, and liraglutide (non-PBS).

GLP-1As work by acting as agonists on GLP-1 receptors. In the pancreas, this enhances glucose-dependent insulin release and reduces glucagon secretion. Actions in the central nervous system and gastrointestinal (GI) tract delay gastric emptying, decrease appetite and delay glucose absorption.¹⁵

In addition to the cardiovascular and renal benefits, GLP-1As may also help weight loss in obesity and reduce non-alcoholic fatty liver disease. This provides an additional treatment option for people living with diabetes with these comorbidities.

GLP-1As have a high incidence of GI adverse effects. Semaglutide may need slow dose escalation to reduce adverse effects. Many patients who experience initial GI adverse effects often find these can settle with ongoing therapy.⁹ Reassure your patient that these effects are expected to reduce over time, and encourage small meals and avoidance of fatty foods. ●



PBS listing

Recent changes in the PBS restrictions have broadened subsidised access to SGLT2 inhibitors. SGLT2 inhibitors can be prescribed using an Authority Required (STREAMLINED) listing for glycaemic control in T2DM, along with CKD and heart failure.¹⁶

To qualify for PBS subsidy for the treatment of T2DM, SGLT2 inhibitors must be used in combination with at least one of metformin, SU, or insulin. SGLT2 inhibitors can also be prescribed as part of triple therapy in combination with metformin and Dipeptidyl peptidase-4 (DPP4) inhibitors, and in quadruple therapy with the addition of insulin.

New initiation of GLP-1As under the PBS requires prescription through the Authority Required (telephone/electronic) listing. Patients who have previously received PBS-subsidised prescription for a GLP-1A can continue to access it through the Authority Required (STREAMLINED) listing.

Patients must be contraindicated, intolerant, or must not have achieved a clinically meaningful glycaemic response to SGLT2 inhibitor to qualify for PBS subsidy. The definition of 'clinically meaningful glycaemic response' can be determined by the prescriber relevant to the patient's individual context.

GLP-1As

- are only subsidised for use in combination with at least one of: metformin, a sulfonylurea, insulin
- are not subsidised for use in combination with a DPP4 inhibitor
- are not subsidised for use in combination with an SGLT2 inhibitor, except where the SGLT2 inhibitor is prescribed for a different indication (e.g., heart failure or kidney disease) and the patient did not achieve a clinically meaningful glycaemic response to the SGLT2 inhibitor.

All T2DM medicines are available for 60-day prescriptions, except GLP-1As and insulin.

Visit PBS for the [full list of recent changes](#). >



PBS restriction changes to type 2 diabetes mellitus (T2DM) medicines



SGLT2 inhibitors and GLP-1As cannot be used in combination if they are both prescribed for glycaemic control in T2DM. However, they can be used in combination with metformin if the SGLT2 inhibitor is prescribed for the management of heart failure or CKD.

What is the role of older classes of medicines?

DPP4 inhibitors (e.g alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin) and SU (e.g gliclazide, glimepiride, glipizide and glibenclamide) can continue if HbA1c is at target, there are no comorbidities of concern, and you are not particularly concerned about side effects or hypoglycaemia.⁵

DPP4 inhibitors do not improve cardiovascular outcomes and are only modestly effective at reducing HbA1c. Saxagliptin can increase the risk of hospitalisation for heart failure in patients with, or with risk factors for, cardiovascular disease.¹⁷ SU increase the risk of hypoglycaemia and weight gain and do not improve cardiovascular outcomes. Acarbose or pioglitazone are used infrequently due to adverse effects and availability of better options.

Insulin still has an important role in managing type 2 diabetes especially if the HbA1c remains high despite lifestyle and medical therapy. It remains the most effective agent at rapidly achieving glycaemic control when there is poor glucose control or if the patient is symptomatic of hyperglycaemia. Consider referral to an endocrinologist if you are dealing with significant clinical complexity, if the patient is not meeting targets after trying different therapies or where the diagnosis is unclear. >



Supporting patients to achieve best outcomes

Organise a GP management plan (MBS items 721 to 732) and provide a structured patient-centred care plan, including team care arrangements (or multidisciplinary care plan for a resident in an aged care facility) to refer to a dietitian, physiotherapist and/or exercise physiologist.

Credentialed diabetes educators can be accessed via these plans and are a valuable resource helping patients understand their medicines and reinforcing lifestyle interventions and self-management strategies.

Refer patients for a Home Medicines Review (HMR – MBS item 900) or Residential Medication Management Review (RMMR – MBS item 903) to check patient’s understanding of diabetes medicines, side effects and adherence to current therapeutics.

Complete a diabetes annual cycle of care.

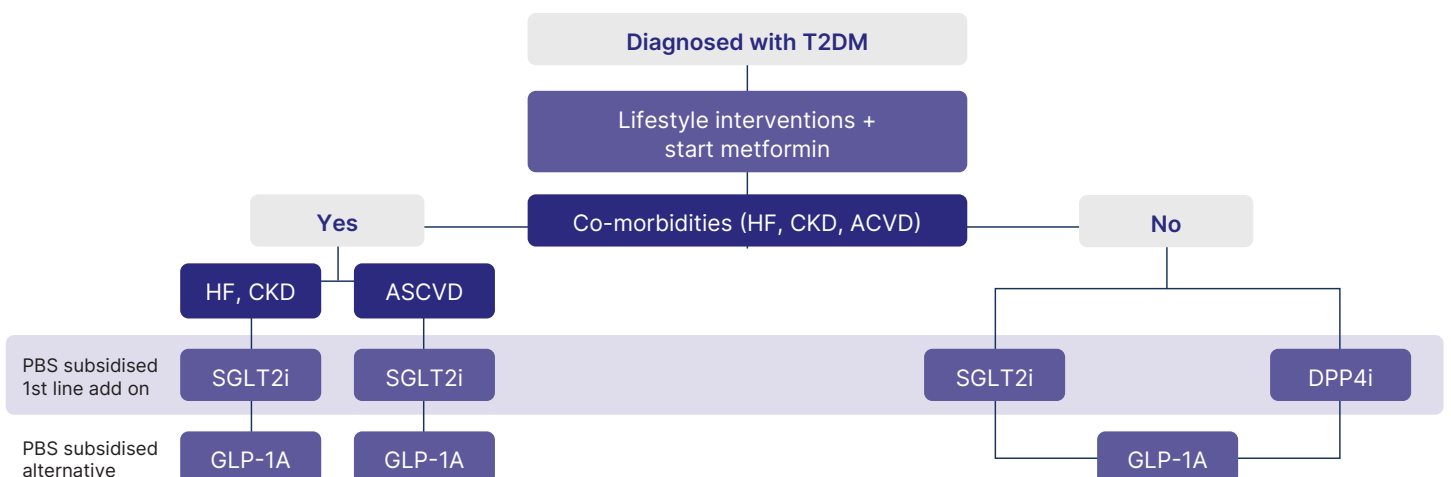
Simplifying treatment for type 2 diabetes

Visit the Australian Diabetes Society for full treatment [glycaemic management in T2DM algorithm](#). ●



glycaemic management in T2DM algorithm

Figure 1: Adapted from guide developed by Associate Professor Gary Kilov.*



*Combined use of an SGLT2 inhibitor and GLP-1As is only eligible for PBS subsidy if the SGLT2 inhibitor is prescribed for heart failure or CKD.

Take home messages

- Always reinforce the benefits of lifestyle intervention and the need for exercise and diet modification throughout the course of the disease.

- Consider the non-glycaemic benefits of SGLT2 inhibitors and GLP-1A in patients with comorbidities.

- Changes to the PBS restrictions allow for a more intensive approach to control of glycaemia and cardio-renal complications with the use of SGLT2 inhibitors.

- Advise your patients about possible adverse effects and how to manage them including making sick day plans and preparing for elective surgery.

- Refer patients for a HMR, create a GP management plan and remember to complete an annual diabetes cycle of care.

- This is a constantly evolving area - evidence is rapidly accumulating and guidelines frequently changing.



For a list of useful links and reference list, please visit our website [MedicinesAdvice.net.au](https://www.MedicinesAdvice.net.au)

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MAIA is funded by the Australian
Government through the Quality Use
of Diagnostics, Therapeutics and
Pathology Program.



Australian Government
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