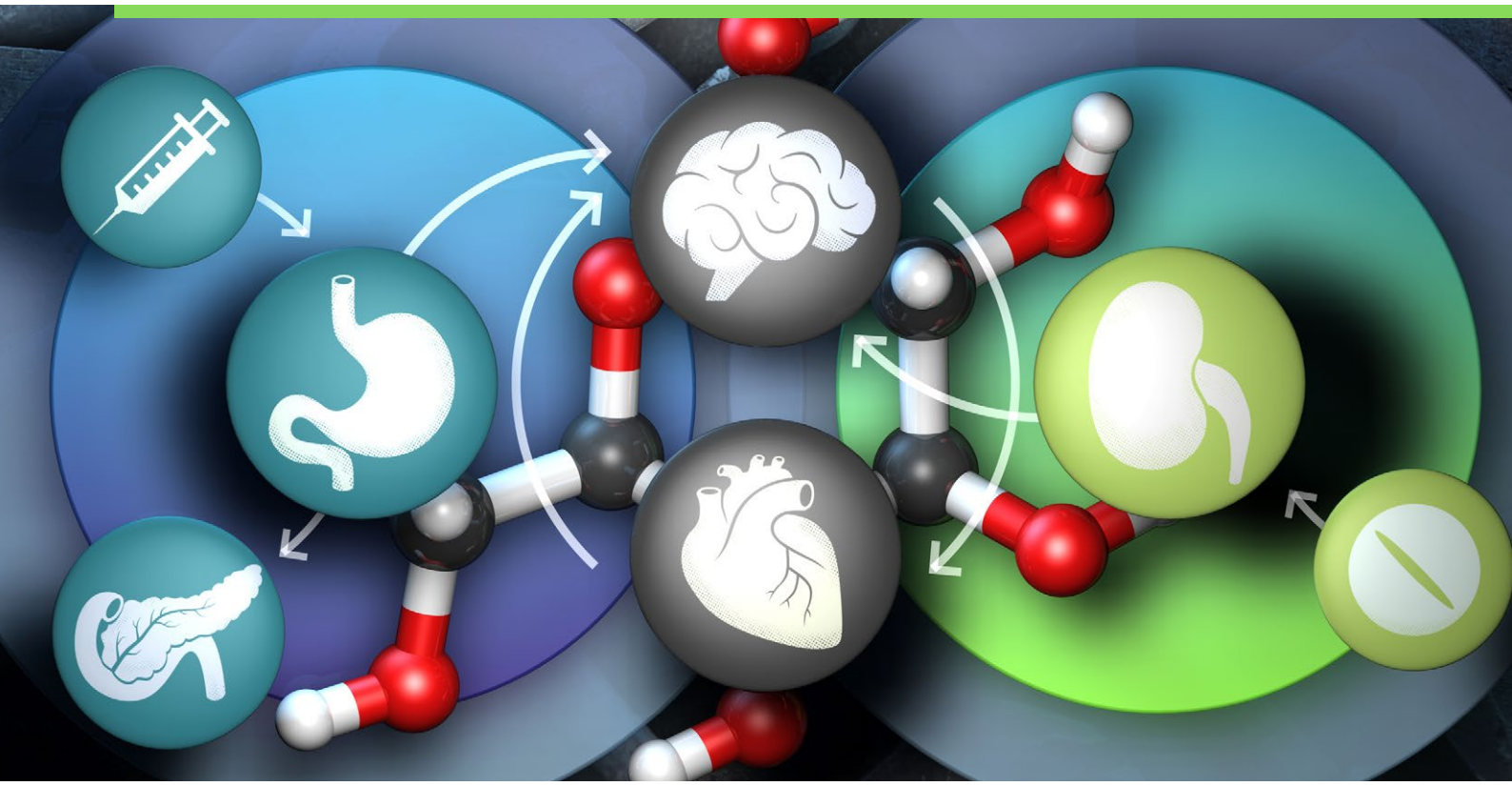

New diabetes medicines funded: **empagliflozin and dulaglutide**

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists have been recommended for the treatment of type 2 diabetes for some time, but until now have not been funded in New Zealand. As of 1 February, 2021, empagliflozin, a SGLT-2 inhibitor, is available fully funded for the treatment of people with type 2 diabetes who are at high risk of cardiovascular disease or have renal complications, including all Māori and Pacific peoples. Dulaglutide, a GLP-1 receptor agonist, is available fully funded from 1 September, 2021.

KEY PRACTICE POINTS:

- Lifestyle interventions, i.e. diet and exercise to achieve weight loss, and metformin remain the cornerstone of type 2 diabetes management
- Empagliflozin, an oral SGLT-2 inhibitor (with or without metformin) and dulaglutide, an injectable GLP-1 receptor agonist, are newly funded options for eligible people with type 2 diabetes to add to lifestyle interventions and metformin
- Empagliflozin and dulaglutide are funded for people with HbA_{1c} levels > 53 mmol/mol who are at high risk of, or with established, cardiovascular disease, diabetic kidney disease, heart failure or who are of Māori or Pacific ethnicity. Dual treatment with these medicines is not funded, although some patients may choose to self-fund.
- Empagliflozin and dulaglutide reduce the risk of cardiovascular and renal complications in people with type 2 diabetes; empagliflozin in particular reduces hospital admission with heart failure. Both classes of medicine also promote weight loss, especially dulaglutide.
- Adverse effects of SGLT-2 inhibitors such as empagliflozin include polyuria and urogenital infections. This medicine class also increases the risk of diabetic ketoacidosis; discuss this risk with patients when initiating treatment and inform them of the key symptoms and signs that should prompt them to seek medical advice.
- Adverse effects of GLP-1 receptor agonists such as dulaglutide include gastrointestinal disturbance and injection site reactions

More tools for the diabetes management toolbox

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists have been recommended internationally in type 2 diabetes management guidelines for some time, but, until now, have been inaccessible to most people in New Zealand due to cost. As of 1 February, 2021, **empagliflozin** (with and without metformin), an oral SGLT-2 inhibitor, is available fully funded with Special Authority approval (see: "Initiating funded treatment").[1] **Dulaglutide**, an injectable GLP-1 receptor agonist, is available fully funded from 1 September, 2021.[1] Both medicines will be the sole subsidised brands until at least 2024.[1]

SGLT-2 inhibitors lower blood glucose levels by inhibiting glucose reabsorption in the renal tubule. In contrast, GLP-1 receptor agonists lower blood glucose levels by stimulating insulin secretion after meals. When added to metformin, SGLT-2 inhibitors and GLP-1 receptor agonists may reduce HbA_{1c} levels by a further 7 to 15 mmol/mol.[2–4]

For further information on the decision to fund these medicines, see: **pharmac.govt.nz/news-and-resources/consultations-and-decisions/decision-to-fund-two-new-medicines-for-type-2-diabetes/**

People at high risk of cardiovascular and renal complications will benefit

Several large randomised controlled trials (RCTs) have shown that treatment with a SGLT-2 inhibitor or GLP-1 receptor agonist provides significant cardiovascular benefit to people with type 2 diabetes.[5] A recent meta-analysis of 764 RCTs including 421,346 people with type 2 diabetes found that both medicine classes reduced:[6]

- All-cause mortality
- Cardiovascular mortality
- Non-fatal myocardial infarction
- Kidney failure

The mechanism by which these medicines reduce adverse cardiovascular outcomes remains uncertain; trials are currently underway to explore the pathways involved, including investigating reductions in oxidative stress and cardiac pre-load.[7]

Table 1 describes the estimated absolute difference in outcomes with SGLT-2 inhibitors and GLP-1 receptor agonists compared with placebo per 1,000 people with type 2 diabetes with moderate or very high cardiovascular risk.[6]*

* Moderate risk defined as people with cardiovascular disease; very high risk defined as people with both cardiovascular disease and chronic kidney disease

Funding criteria is intended to help reduce inequities

For the first time, Māori and Pacific peoples have been specifically identified within Special Authority criteria for funding (see: "Initiating funded treatment" for the full criteria). The prevalence of type 2 diabetes is two to three times higher in these ethnic groups than others.[8] Māori and Pacific peoples with type 2 diabetes have worse health outcomes compared to Europeans.[9, 10] Improved access to medicines with established cardiovascular and renal benefits is hoped to reduce the inequities in diabetes health outcomes in these populations.

Table 1. Estimated absolute differences in outcomes with SGLT-2 inhibitors and GLP-1 receptor agonists compared with placebo per 1,000 people with type 2 diabetes with moderate and very high cardiovascular risk, treated for five years. Adapted from Palmer et al. (2021).[6]

	CVD risk category*	All-cause mortality	Cardiovascular mortality	Non-fatal myocardial infarction	Non-fatal stroke	Kidney failure	Hospital admission for heart failure
SGLT-2 inhibitor	Moderate	25 fewer (32 fewer – 18 fewer)	12 fewer (18 fewer – 6 fewer)	13 fewer (21 fewer – 3 fewer)	1 more (11 fewer – 13 more)	6 fewer (9 fewer – 2 fewer)	23 fewer (28 fewer – 17 fewer)
	Very high	48 fewer (61 fewer – 35 fewer)	24 fewer (36 fewer – 12 fewer)	21 fewer (34 fewer – 5 fewer)	2 more (17 fewer – 21 more)	38 fewer (58 fewer – 14 fewer)	58 fewer (73 fewer – 44 fewer)
GLP-1 receptor agonist	Moderate	13 fewer (18 fewer – 6 fewer)	9 fewer (15 fewer – 1 fewer)	8 fewer (15 fewer – 1 fewer)	16 fewer (24 fewer – 7 fewer)	4 fewer (7 fewer – 2 fewer)	4 fewer (11 fewer – 2 more)
	Very high	24 fewer (35 fewer – 12 fewer)	18 fewer (30 fewer – 6 fewer)	13 fewer (24 fewer – 2 fewer)	25 fewer (39 fewer – 11 fewer)	29 fewer (44 fewer – 10 fewer)	11 fewer (28 fewer – 5 fewer)

* Moderate risk defined as people with CVD; very high risk defined as people with both CVD and chronic kidney disease

The place of empagliflozin and dulaglutide in type 2 diabetes management

Type 2 diabetes management follows a stepwise progression. Lifestyle interventions and metformin are the cornerstone of type 2 diabetes management (Step 1). If a sufficient reduction in HbA_{1c} levels is not achieved with metformin, treatment is typically escalated by reinforcing the importance of diet and exercise to induce weight loss, and adding a second non-insulin pharmacological treatment (Step 2a). If further intensification is required, a third non-insulin pharmacological treatment can be added (Step 2b) or insulin can be initiated (Step 3).

N.B. Consider starting at Step 2 at diagnosis for patients with HbA_{1c} levels > 64 mmol/mol, i.e. two pharmacological treatments (e.g. metformin and vildagliptin) and lifestyle management.[11] Consider initiating insulin at diagnosis if very high HbA_{1c} levels, e.g. > 80 – 90 mmol/mol*, or significant symptoms of hyperglycaemia.[11] Insulin may be withdrawn once HbA_{1c} levels are controlled.

* This is a higher level than in previous guidance (75 mmol/mol) due to the availability of more medicines to manage hyperglycaemia[12]

Treatment options at Step 2 (typically added to metformin) include:

- **Empagliflozin** (oral, funded with Special Authority – see: "Initiating funded treatment" and "Prescribing empagliflozin"), taken either as separate metformin and empagliflozin tablets, or a combination empagliflozin + metformin formulation
- **Dulaglutide** (injectable, funded with Special Authority – see: "Initiating funded treatment" and "Prescribing dulaglutide")
- **Vildagliptin** (oral, funded), taken either as separate metformin and vildagliptin tablets, or a combination vildagliptin + metformin formulation
- A sulfonylurea (oral, funded), such as **gliclazide** or **glipizide**
- **Pioglitazone** (oral, funded)

The decision about which medicine to use should take into account any contraindications, cardiovascular co-morbidities, risk of hypoglycaemia, effects on weight, medicines interactions, adverse effects and eligibility for funding (see: Table 2 and "Initiating funded treatment").[5]

Empagliflozin or dulaglutide are preferred at Step 2 for people with or at high risk of CVD, diabetic kidney disease or heart failure, regardless of their HbA_{1c} levels; currently only people with HbA_{1c} levels > 53 mmol/mol are eligible for funded treatment (see: "Initiating funded treatment").[11] Both medicine classes can be used together with likely additive benefits, however, dual treatment with empagliflozin and dulaglutide is not funded.[11] There is little risk of hypoglycaemia with these medicines without concomitant use of sulfonylureas or insulin.

N.B. A SGLT-2 inhibitor or GLP-1 receptor agonist are also preferred in some international guidelines if there is a need to minimise weight gain or promote weight loss, however, they are not funded for these indications in New Zealand.[5,13]

Table 2. Effects of diabetes medicines (excluding insulin) on HbA_{1c}, cardiovascular co-morbidities, progression of kidney disease, weight and risk of hypoglycaemia and diabetic ketoacidosis. Adapted from the American Diabetes Association (2021) and NZSSD (2021).[5, 11]

Medicine	Efficacy for lowering HbA_{1c}	Cardiovascular effects		Renal effects: progression of DKD	Effects on weight	Risk of hypoglycaemia	Risk of DKA
		CVD	HF				
Metformin	High	Potential benefit	Neutral	Neutral	Neutral with potential for modest loss	Low	Low
Empagliflozin	Intermediate	Benefit	Benefit	Benefit	Loss	Low	High
Dulaglutide	High	Benefit	Neutral	Benefit	Loss	Low	Low
Vildagliptin	Intermediate	Neutral	Neutral	Neutral	Neutral	Low	Low
Sulfonylureas	High	Neutral	Neutral	Neutral	Gain	High	Low
Pioglitazone	High	Potential benefit	Increased risk	Neutral	Gain	Low	Low

CVD = cardiovascular disease HF = heart failure DKD = diabetic kidney disease DKA = diabetic ketoacidosis

Clinical scenarios where empagliflozin or dulaglutide are recommended, but not funded

The recently released type 2 diabetes management guidelines developed by the New Zealand Society for the Study of Diabetes (NZSSD), and supported by the Ministry of Health, states that while the Special Authority criteria for empagliflozin and dulaglutide ensure access for those at high risk of cardiovascular and renal disease, the funding restriction is not fully consistent with best practice.[11]

Patients with type 2 diabetes who are likely to benefit from these medicines but who do not meet the criteria for funded treatment are those:[11]

- With CVD (or five-year CVD risk ≥ 15%), renal disease or heart failure with a HbA_{1c} < 53 mmol/mol or eGFR 60 – 90 mL/min/1.73 m^2 without albuminuria
- With CVD (or five-year CVD risk ≥ 15%), renal disease or heart failure who are already taking funded empagliflozin or dulaglutide (i.e. dual treatment with these medicines is recommended, but only one can be funded at a time)
- Who are overweight or obese and have HbA_{1c} levels above target despite regular use of or inability to tolerate metformin, but who do not have cardiovascular or renal disease and are not of Māori or Pacific ethnicity
- With a HbA_{1c} above target despite regular use of or inability to tolerate metformin and vildagliptin, but who do not have cardiovascular or renal disease and are not of Māori or Pacific ethnicity
- With a HbA_{1c} within the target range but where a SGLT-2 inhibitor is preferred to reduce adverse effects, e.g. weight gain or hypoglycaemia with a thiazolidinedione or sulfonylurea, respectively

Discuss the recommendation with patients and the option to self-fund treatment, unless there are contraindications or significant cautions. This may be a challenging conversation to negotiate as there will be patients who are unable to meet the financial burden of self-funding treatment and may find this distressing.

Vildagliptin is recommended at Step 2 for people with type 2 diabetes who are not eligible for funded SGLT-2 inhibitor or GLP-1 receptor agonist treatment (also see: "Clinical scenarios where empagliflozin or dulaglutide are recommended, but not funded").[11] Vildagliptin is particularly useful in older patients, either combined with metformin or alone if metformin is contraindicated or not tolerated.

A new type 2 diabetes management guideline published by the New Zealand Society for the Study of Diabetes and the Ministry of Health is available here: **t2dm.nzssd.org.nz/**

Initiating funded treatment

To initiate funded empagliflozin or dulaglutide treatment, patients must have type 2 diabetes and meet **all** of the following criteria:[1]

1. Have at **least one** of the following characteristics:
   a) Māori or any Pacific ethnicity; or
   b) Pre-existing CVD or risk equivalent*; or
   c) An absolute five-year CVD risk of ≥ 15% according to a validated cardiovascular risk assessment calculator; or
   d) A high lifetime cardiovascular risk due to being diagnosed with type 2 diabetes during childhood or as a young adult; or
   e) Diabetic kidney disease†; and
2. HbA_{1c} level > 53 mmol/mol despite the regular use of at least one blood-glucose lowering agent (e.g. metformin, vildagliptin or insulin) for at least three months;** and
3. Treatment will not be used in combination with a funded GLP-1 receptor agonist/SGLT-2 inhibitor (as appropriate)

* Defined as: prior cardiovascular disease event (i.e. angina, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, transient ischaemic attack, ischaemic stroke, peripheral vascular disease), congestive heart failure or familial hypercholesterolaemia

† Defined as: persistent albuminuria (albumin:creatinine ratio greater than or equal to 3 mg/mmol, in at least two out of three samples over a 3 – 6-month period) and/or eGFR less than 60 mL/min/1.73m^2 in the presence of diabetes, without alternative cause

** If HbA_{1c} is very high at diagnosis, e.g. > 64 mmol/mol, they would not be eligible for funded treatment with empagliflozin or dulaglutide until they have been treated with at least one glucose-lowering agent for three months; patients with high HbA_{1c} at diagnosis could be initiated on metformin + vildagliptin or, if HbA_{1c} are very high at diagnosis, metformin and insulin (which could then be withdrawn once HbA_{1c} has stabilised)

Applications can be made by any relevant practitioner and are valid without further renewal (unless notified) for eligible patients.

A calculator to assess cardiovascular disease risk in people with type 2 diabetes is available here: **www.nzssd.org.nz/calculators/calculator/1/cvd-risk-assessment**

Choosing between empagliflozin and dulaglutide

The decision to initiate a SGLT-2 inhibitor versus a GLP-1 receptor agonist is based primarily on the predominant co-morbidity, i.e. CVD, heart failure or diabetic kidney disease, and patient preference, particularly regarding the route of administration (Figure 1).[11] If heart failure or diabetic kidney disease predominates, a SGLT-2 inhibitor (i.e. empagliflozin) is preferred. Otherwise either a SGLT-2 inhibitor or a GLP-1 receptor agonist (i.e. dulaglutide) is recommended; GLP-1 receptor agonist treatment will likely lead to greater improvements in glycaemic control and greater weight loss than SGLT-2 inhibitor treatment (although SGLT-2 inhibitors are still associated with weight loss).[11]

An interactive decision support tool for choosing between a SGLT-2 inhibitor and GLP-1 receptor agonist is available here: **magicevidence.org/match-it/200820dist**

Dulaglutide is administered as a once weekly injection

Patients may be reluctant to take dulaglutide as it is an injectable treatment rather than an oral medicine. However, unlike insulin, which requires one or more daily injections, dulaglutide is administered once weekly. Furthermore, self-monitoring blood glucose is not necessary for patients taking dulaglutide, unless their regimen also includes a sulfonylurea or insulin. Providing patients who are hesitant about initiating an injectable treatment with this information may help them to feel more confident with this treatment option. A treatment trial of dulaglutide may be very useful before initiating insulin.

Prescribing empagliflozin

When initiating empagliflozin, reinforce lifestyle advice, i.e. dietary and exercise interventions, and offer support as required. Metformin should be continued unless it is contraindicated or not tolerated; combination empagliflozin + metformin formulations are available (Table 3).[11] Other glucose-lowering treatments (e.g. vildagliptin, a sulfonylurea, dulaglutide,* or insulin) should be continued if needed for glycaemic control or cardiovascular or renal protection.[11] If the patient is taking insulin or a sulfonylurea, the dose may need to be reduced; a reduction of 15 – 20% of the daily total insulin or 50% of the sulfonylurea dose is recommended as a starting point.[11] People with a HbA_{1c} > 75 mmol/mol do not usually require a reduction in insulin or sulfonylurea, unless they have a history of hypoglycaemia.[11] Patients taking SGLT-2 inhibitors must discontinue treatment during an acute illness or three days before an elective medical procedure.[11]

* Dual empagliflozin and dulaglutide treatment is not currently funded under the Special Authority criteria

Table 3. Key empagliflozin prescribing information.[11, 14, 15]

	Formulation	Dose information	Notes
Empagliflozin	10 mg and 25 mg, tablet	▪ Initiate at 10 mg daily ▪ Increase to maximum of 25 mg daily after several weeks if no adverse effects AND as required for glycaemic control	▪ Contraindicated for people with eGFR < 30 mL/min/1.73 m^2 as it is ineffective in reducing glucose levels* ▪ No dose adjustment required for people with mild renal impairment
Empagliflozin with metformin hydrochloride	5 mg empagliflozin with 500 mg or 1000 mg metformin, tablet	▪ Initiate at 5 mg empagliflozin twice daily (10 mg total daily dose); choose the dose of metformin similar to the dose already being taken	▪ Contraindicated for people with eGFR < 30 mL/min/1.73 m^2 due to metformin component and the ineffectiveness of the empagliflozin component
	12.5 mg empagliflozin with 500 mg or 1000 mg metformin, tablet	▪ Maximum recommended daily dose is 25 mg empagliflozin and 2000 mg metformin	▪ Reduce metformin dose for people with renal impairment; no empagliflozin dose adjustment is required for people with mild renal impairment

* It may assist kidney function, but this has not been definitively proven

At diagnosis:

Discuss non-pharmacological treatment:

- Lifestyle changes are the cornerstone of management; emphasise the importance of diet and exercise approaches regardless of which medicines are used
- Support and encourage patients to make lifestyle changes throughout follow-up
- Refer patients to support services, e.g. Green Prescription or dietitian, to assist with lifestyle changes

Determine an appropriate HbA_{1c} target:

Prescribe an appropriate medicine regimen based on the extent of hyperglycaemia:

- Initiate metformin at, or soon after diagnosis, unless contraindicated
- Consider initiating two pharmacological treatments at diagnosis (e.g. metformin and vildagliptin) if HbA_{1c} > 64 mmol/mol
- Consider initiating insulin at diagnosis if patients have high HbA_{1c} levels at diagnosis, e.g. > 80 – 90 mmol/mol

Escalating treatment:

DKD* or HF or known CVD or five-year CVD risk ≥ 15%?

* DKD = urinary albumin:creatinine ratio > 3 mg/mmol and/or reduced eGFR

Yes

HF or DKD predominates?

Yes

SGL T-2 inhibitor preferred
(i.e. empagliflozin)†

No

GLP-1 receptor agonist
(i.e. dulaglutide)†
or **SGL T-2 inhibitor**
(i.e. empagliflozin)†

Treatment not tolerated or HbA_{1c} above target

Add another pharmacological treatment:

- GLP-1 receptor agonist preferred treatment to add to SGLT-2 inhibitor
- SGLT-2 inhibitor preferred treatment to add to GLP-1 receptor agonist

N.B. Dual SGLT-2 inhibitor/GLP-1 receptor agonist treatment not currently funded

Alternatives:

- Vildagliptin, if not on GLP-1 receptor agonist
- Pioglitazone (unless heart failure)
- A sulfonylurea
- Insulin

No

Add another pharmacological treatment:

- SGLT-2 inhibitor†
- GLP-1 receptor agonist†
- Vildagliptin

Alternatives:

- Pioglitazone
- A sulfonylurea
- Insulin

† Special Authority criteria apply; dulaglutide availability subject to Medsafe approval

DKD = diabetic kidney disease

HF = heart failure

CVD = cardiovascular disease

Figure 1. An overview of management of patients with type 2 diabetes. Adapted from the New Zealand Society for the Study of Diabetes type 2 diabetes guideline (2021).[11]

For further information on sick-day management, see: **t2dm.nzssd.org.nz/Section-95-Sick-day-management-in-patients-with-diabetes**

Contraindications and cautions to empagliflozin treatment

Empagliflozin is currently contraindicated in people with severe renal impairment; it is ineffective at lowering glucose if eGFR < 30 mL/minute/1.73 m^2. Empagliflozin is not recommended for use in people who:[11]

- Are aged < 18 years
- Are pregnant or breastfeeding
- Have a history of severe genitourinary infections
- Are on a ketogenic diet (due to the increased risk of diabetic ketoacidosis – see below)

N.B. Use of empagliflozin in people with nephrolithiasis/recurrent renal calculi was previously not recommended in the NZSSD guidance. However, updated advice is that empagliflozin may be used with caution in patients with a history of renal calculi if good hydration is ensured; extra caution is needed in those with recurrent calculi.

For further information, refer to the New Zealand Formulary: **www.nzf.org.nz/nzf_70809**

Discuss potential adverse effects before initiating treatment

Adverse effects of SGLT-2 inhibitors such as empagliflozin include:[11]

- Polyuria – consider reducing diuretics before initiating treatment
- Genitourinary infections, e.g. urinary tract infection, vaginal thrush, balantitis – this is thought to be due to the increased urinary excretion of glucose. Ensure patients are given information on hygiene measures and the rare risk of necrotising fasciitis of the perineum (Fournier's gangrene).
- Hypotension – consider reducing antihypertensive medicines before initiating treatment or before a dose increase
- Diabetic ketoacidosis (DKA) – increased risk (see below)

SGLT-2 inhibitor use is associated with an increased risk of severe DKA

People taking SGLT-2 inhibitors are at increased risk of DKA, particularly in the first few months of treatment or peri-operatively.[11] **This can occur with normal blood glucose levels (euglycaemia).**[11] While this is a rare adverse effect (ranging from one in 1,000 to one in 3,000 people), this should be discussed with patients before initiating treatment, with advice provided on the symptoms and signs of DKA and when to seek medical attention to get their blood ketones checked (i.e. if they experience nausea, vomiting or abdominal pain).[11] In general, it is advisable to temporarily stop empagliflozin if patients are unwell and febrile, especially if they are not eating or vomiting.

N.B. Patients with type 2 diabetes taking a SGLT-2 inhibitor do not currently qualify for a funded CareSens Dual glucometer (measures both blood glucose and blood ketone levels).

For further information on SGLT-2 inhibitors and DKA, see: **diabetessociety.com.au/documents/ADS_DKA_SGLT2i_Alert_update_2020.pdf**

Prescribing dulaglutide

Dulaglutide, a GLP-1 receptor agonist, was approved by Medsafe on 12 August, 2021, and is funded from 1 September, 2021 (with Special Authority). Refer to the NZF for further information: **nzf.org.nz/nzf_71107**

When initiating dulaglutide, reinforce lifestyle advice and offer support as required, and provide information on how to administer treatment (see below). Metformin should be continued unless it is contraindicated or not tolerated.[11] Dipeptidyl peptidase-4 (DPP-4) inhibitors (i.e. vildagliptin) must be stopped before initiating a GLP-1 receptor agonist as they have similar mechanisms of action.[11] Other glucose-lowering treatments can be continued if needed for glycaemic control or cardiovascular or renal protection, with the dose of insulin or a sulfonylurea reduced to prevent hypoglycaemia, if required (see: "Prescribing empagliflozin" for guidance on dose reduction).[11] Advise patients to stop treatment if they have an acute gastrointestinal illness (and resume treatment once they have recovered).[11]

Table 4. Key dulaglutide prescribing information.[11, 16]

Funded GLP-1 receptor agonist*	Formulation	Dose information
Dulaglutide	1.5 mg per 0.5 ml prefilled pen, injectable	■ Administered subcutaneously, once weekly; each pen contains one dose of dulaglutide and should only be used once

* Other non-funded GLP-1 receptor agonists approved in New Zealand include liraglutide, exenatide and exenatide extended release (soon to be withdrawn from the local market)

Dulaglutide administration guide:[16]

- Dulaglutide is administered once weekly, at any time of day, with or without food
- Patients can inject dulaglutide in the abdomen, thigh or upper arm
- Injection sites should be rotated with each dose
- If a dose is missed, it should be administered as soon as possible if there are ≥ 3 days until the next scheduled dose; if < 3 days until the next dose, the missed dose should not be taken, and the next dose taken at the normal time
- If the regimen includes insulin, these should be administered as separate injections, i.e. not mixed. If injected in the same body region, ensure the injections are not next to each other.
- The single-use pen should be disposed of in a specified sharps container or a closable puncture-resistant container, i.e. not in the household rubbish*

* Community pharmacies and some Diabetes NZ branches offer sharps disposal services; patients can return their sharps in a specified sharps container (available to purchase) or other suitable container

Patient instructions for use of dulaglutide (with images) are available from: **uspl.lilly.com/trulicity/trulicity.html#ug**

Contraindications and cautions to dulaglutide treatment

Dulaglutide is contraindicated in people with personal or family history of medullary thyroid carcinoma or a personal history of multiple endocrine neoplasia syndrome type 2.[11, 16] Rodent studies have shown an increased incidence of thyroid C-cell adenomas and carcinomas with GLP-1 receptor agonist treatment.[17] While a causal relationship has not been established and there is no evidence of increased prevalence of any form of thyroid cancer in humans with long-term use, dulaglutide is not recommended for use in people at increased risk of thyroid cancer, e.g. due to family history, radiation exposure.[11] Advise patients prescribed dulaglutide to seek medical advice if they develop any symptoms that could indicate thyroid cancer, e.g. a mass in the neck, dysphagia, dyspnoea, persistent hoarseness.[16]

Dulaglutide is not recommended for people:[11]

- Aged < 18 years
- Who are pregnant or breastfeeding
- With severe gastrointestinal disease, including gastroparesis
- With previous pancreatitis

Mild adverse effects with dulaglutide are usually transient

Common adverse effects of GLP-1 receptor agonists include gastrointestinal disturbance (nausea [most common], vomiting, anorexia and diarrhoea) and injection site reactions (e.g. nodules, pruritus, bruising, erythema).[11, 18] These are usually transient and improve with continued treatment.[11] Rare adverse effects include pancreatitis, myalgias and muscle weakness, Stevens-Johnson's syndrome and thromocytopaenia.[11]

Reviewing treatment and ongoing monitoring

Regular review of treatment is necessary for all patients with type 2 diabetes to optimise individual goals and ensure medicine regimens remain appropriate. Nutrition, physical activity and body weight monitoring should be discussed with patients at all stages of management. HbA_{1c} levels should be checked every three months if they are above target and the treatment regimen has changed.[11] Once target HbA_{1c} levels have been achieved, repeat measurement every six months and complete a diabetes review annually.[11] Renal function should be assessed at least annually in patients taking empagliflozin (with or without metformin) and prior to initiating any medicines that may reduce renal function.[14] No additional monitoring is required for patients taking dulaglutide.

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