Initiating treatment with dulaglutide or liraglutide

in adult patients with type 2 diabetes

Algorithms,
notes and talking points

Getting started

When clinically indicated, a glucagon-like peptide 1 receptor agonist (GLP1RA) can be started **in adult patients with type 2 diabetes** using the steps shown in this resource.

Note: Dulaglutide and liraglutide (Victoza, not Saxenda) are the only registered and funded GLP1RAs for type 2 diabetes in Aotearoa New Zealand.

Talking points, relevant for all patients starting a GLP1RA, are provided along with two algorithms and accompanying notes. Which algorithm you follow will depend on your patient's level of hypoglycaemia risk. Always maintain metformin treatment if tolerated.

Follow Algorithm 1 if your patient is not using a sulfonylurea or insulin. They will have no significant risk of developing hypoglycaemia when starting a GLP1RA.

Follow Algorithm 2 if your patient is currently using a sulfonylurea or insulin. They will have a risk of developing hypoglycaemia when starting a GLP1RA.

This resource is intended to guide prescribers through the process of starting a GLP1RA in adult patients with type 2 diabetes. A similar resource has been developed for initiating the sodium–glucose cotransporter-2 (SGLT2) inhibitor, empagliflozin. At the time of writing, only one of these agents can be funded on Special Authority for any one patient.

When deciding whether a GLP1RA (dulaglutide, Victoza liraglutide) or an SGLT2 inhibitor (empagliflozin) would be most suitable for your patient, consider that:

- A GLP1RA is typically the choice for patients in whom cerebrovascular or cardiovascular disease or risk predominates, particularly in the setting of higher HbA1c or motivation to lose weight.
- An SGLT2 inhibitor is typically the choice for patients in whom heart failure (particularly with reduced ejection fraction) or diabetic kidney disease predominates.

If tolerability of one of these medicines becomes an issue, one of the other funded options can be considered.

For further, comprehensive information on using GLP1RAs in type 2 diabetes, visit the New Zealand Society for the Study of Diabetes (NZSSD) at www.nzssd.org.nz

Talking points

The following are key talking points for you to cover with patients starting a GLP1RA.

Patient information can be printed from www.healthnavigator.org.nz/medicines

Benefits and harms[1, 2]

Expected benefits – in brief, dulaglutide and liraglutide:

- reduce HbA1c
- reduce the risk of non-fatal myocardial infarction (heart attack), non-fatal stroke or death from cardiovascular causes in patients with cardiovascular disease (CVD). Dulaglutide is also effective in the primary prevention of CVD events.
- reduce blood total cholesterol, LDL-cholesterol and triglyceride levels
- reduce systolic blood pressure
- help preserve renal function (slows decline in GFR and onset of end-stage kidney disease)
- may lead to weight loss
- may delay the need for insulin in the treatment of type 2 diabetes
- carry a low risk of hypoglycaemia – usually only seen when used in combination with a sulfonylurea or insulin.

Potential adverse effects – in brief, dulaglutide and liraglutide can cause:

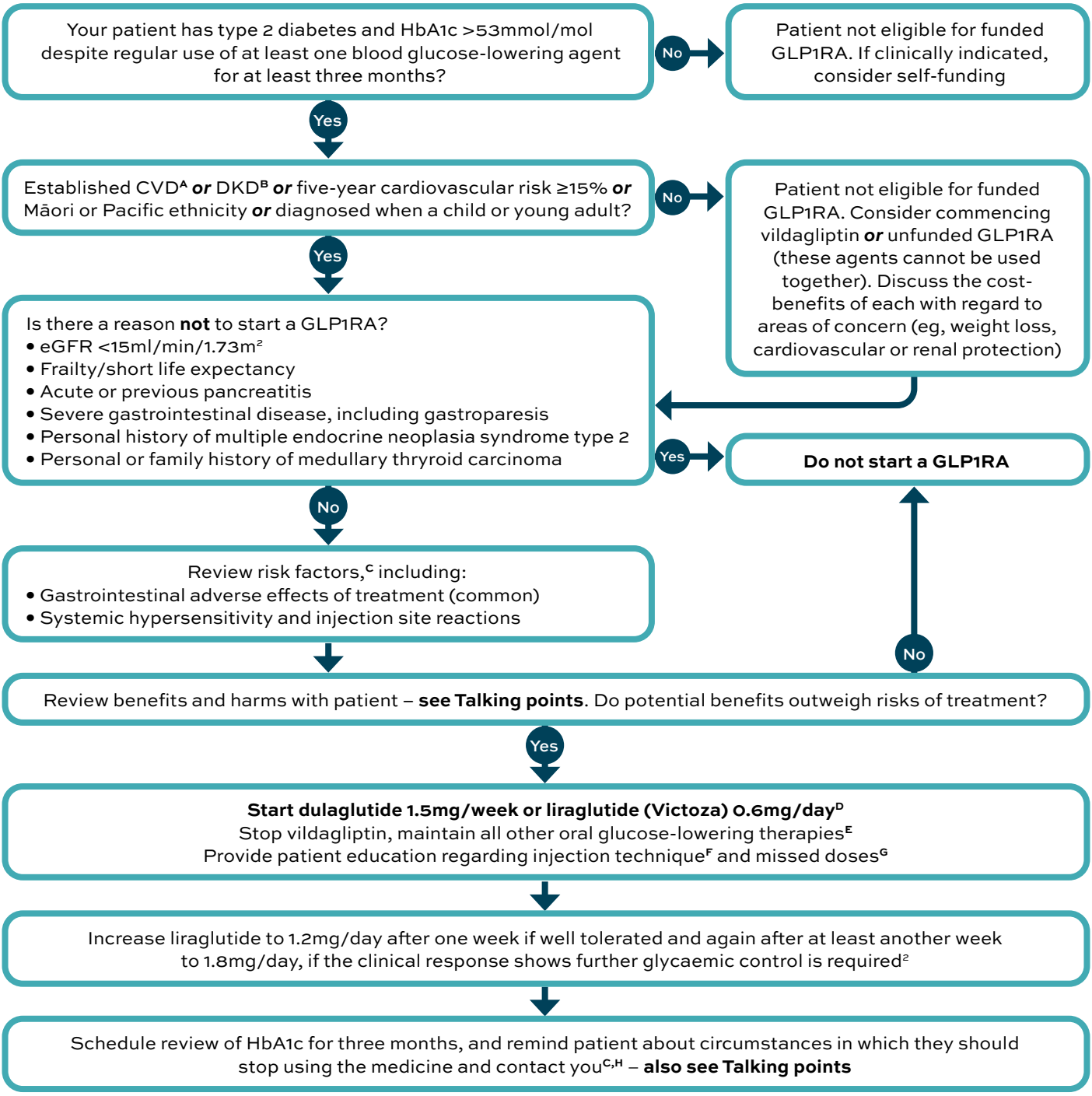
- gastrointestinal adverse effects (most commonly nausea, dyspepsia, diarrhoea and reduced appetite), most pronounced after the initial dose but tending to settle over a few weeks
- more severe gastric disturbance, diarrhoea or vomiting, potentially affecting tolerability of the medicine (suspend use in acute/severe gastrointestinal illness, until it resolves); be alert for persistent, severe abdominal pain with/without vomiting (pancreatitis is rare but its occurrence requires stopping the medicine)
- injection-site reactions such as redness, soreness and swelling, or transient nodules
- systemic hypersensitivity reactions (eg, urticaria, oedema) in about 1 in 200 patients – there are also rare, documented cases of anaphylaxis.

Points to raise with your patients

- Continue your other medicines unless specifically told to stop by your healthcare provider.
- You may be asked to change doses of your other blood glucose-lowering medicines over the next four weeks.
- If also using insulin, inject the GLP1RA to a different site and at a different time if possible. Avoid using sites where a nodule may have developed.
- Drink plenty of fluids and stay well-hydrated, particularly in summer and when exercising.
- Do not over-indulge in alcohol.
- Talk with your healthcare provider if you plan to make dramatic dietary changes (eg, a large change in carbohydrates).
- Regularly check your feet and maintain good foot care.
- Contact your healthcare provider if you notice any infections or rashes.
- Make sure to tell other healthcare professionals that you are taking this medicine.
- **Stop the dulaglutide or liraglutide** if you have severe gastrointestinal illness; persistent, severe stomach pains with or without vomiting; or experience a hypersensitivity reaction causing swelling or fluid accumulation, particularly around the face, lips or tongue – **seek medical advice urgently and contact your healthcare provider**.
- GLP1RAs should be avoided in pregnancy.[3] Contraception may need to be discussed as weight loss in non-ovulating women may lead to a return to normal ovulation.

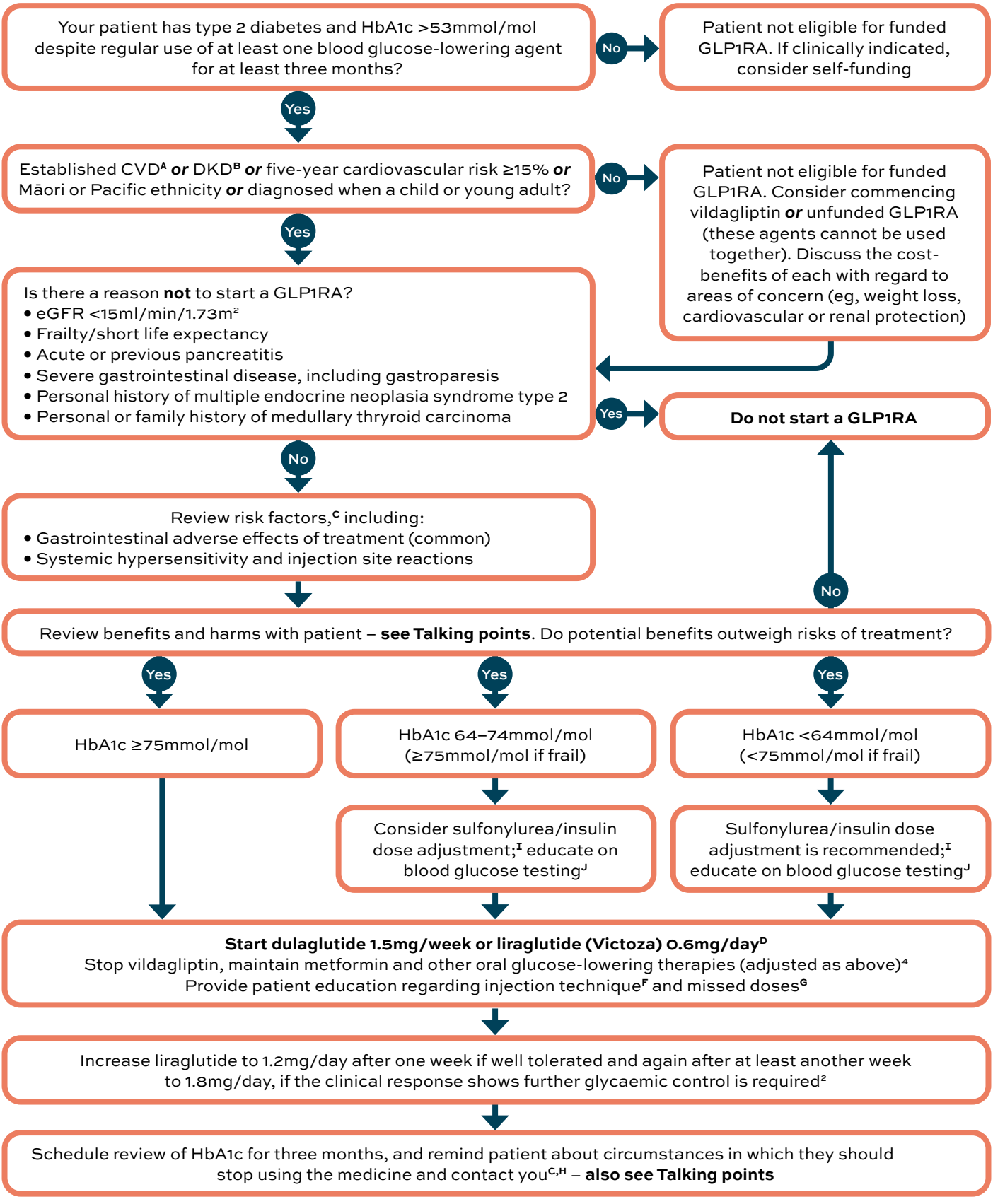
Algorithm 1 – GLP1RA

Type 2 diabetes patients NOT on a sulfonylurea or insulin



Algorithm 2 – GLP1RA

Type 2 diabetes patients on a sulfonylurea or insulin



Additional prescribing notes

A. Established CVD (cardiovascular disease) is defined as a prior CVD event (ie, angina, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, transient ischaemic attack, ischaemic stroke, peripheral vascular disease), congestive heart failure or familial hypercholesterolaemia.[5]

B. Established DKD (diabetic kidney disease) is defined as persistent albuminuria (albumin:creatinine ratio ≥3mg/mmol, in at least two out of three samples over a 3–6 month period) and/or eGFR <60ml/min/1.73m^2 in the presence of diabetes, without alternative cause.[5]

C. Adverse effects to be alert for:[1,2]

- **Gastrointestinal events** (nausea, vomiting, diarrhoea) are common but typically mild or moderate, usually occur within 2–3 days of the first dose, are less severe with subsequent doses and rapidly decline within a few weeks.
  - *Monitor for dehydration and deteriorating renal function: Ensure the patient knows the signs of dehydration and how to manage it. Monitor renal function in patients with renal impairment and severe adverse GI events.*
  - *Stopping a GLP1RA: The patient should suspend use of dulaglutide or liraglutide (Victoza) during acute GI illness and stop it if they develop gastroparesis or symptoms suggesting pancreatitis.*
- **Injection site reactions** such as redness, soreness and swelling, or transient nodules.
- **Systemic hypersensitivity reactions** (eg, urticaria, oedema). Previous hypersensitivity reaction to a GLP1RA is a contraindication for starting dulaglutide or liraglutide. There are rare, documented cases of anaphylaxis.

D. The dose of dulaglutide is 1.5mg once per week subcutaneously, delivered with a single-use pen at any time of day, independent of meals. (1.5mg is the only dulaglutide pen dose available in New Zealand)[5]
The dose of liraglutide (Victoza) is 0.6mg to 1.8mg daily subcutaneously (delivered with a pre-filled multidose, disposable pen) at a regular time of day, independent of meals. The Victoza pen contains 30 doses of 0.6mg, 15 doses of 1.2mg, or 10 doses of 1.8mg.
No dosage adjustment of GLP1RA is required for the elderly or for hepatic or renal impairment, but do not use in patients with eGFR <15ml/min/1.73m^2. Not registered for use in pregnancy, breastfeeding or people <18 years old.[1,2] Phase III study data confirms safety and efficacy in 10–17 year olds, but use would be off-label.[4] Cessation of vildagliptin is essential.[4]

E. If the patient is not on a sulfonylurea or insulin, dosage adjustment of other medicines is not usually required when starting a GLP1RA as the risk of hypoglycaemia is low. Always maintain metformin if tolerated, but vildagliptin must be stopped.[4]

F. Good injection technique involves choosing appropriate injection sites. Inject the dose subcutaneously into the abdomen or thigh, or a partner/carer may inject it into the upper arm. Change (rotate) the injection site each time – the patient may use the same area of their body providing they choose a different injection site within that area.[1,2,6] If also injecting insulin, administer this separately into a different injection site.

G. If a dose of dulaglutide is missed, it should be injected as soon as possible if there are at least 72 hours (three days) until the next scheduled dose. If fewer than three days remain before the next scheduled dose, the missed dose should be skipped and the next dose administered on the regularly scheduled day.[1]
If a dose of liraglutide (Victoza) is missed, it should be injected as soon as possible within 12 hours from the time of the scheduled dose. If more than 12 hours has passed since the dose was missed, it should be skipped and the next scheduled dose injected as planned.[2]

H. For sick day management refer to NZSSD Type 2 Diabetes Management Guidelines: Sick day management in patients with diabetes:[4] tinyurl.com/nzssd-sick-day

I. Consider dosage adjustment of sulfonylurea and insulin based on patient's HbA1c[4]

- **HbA1c <64mmol/mol (<75mmol/mol if frail):** 15–20% insulin dose reduction and 50% sulfonylurea dose reduction (or stop sulfonylurea) recommended when starting a GLP1RA.
- **HbA1c 64–74mmol/mol (≥75mmol/mol if frail):** consider insulin and sulfonylurea dose adjustments based on variability in glycaemic control (if patient monitors blood glucose) or expected reduction and hypoglycaemia risk when starting a GLP1RA.
- May need to switch from premixed insulin to basal insulin alone, or stop low-dose sulfonylureas or bolus insulin, especially if HbA1c <64mmol/mol.[4]

J. Blood glucose monitoring is discussed in detail at tinyurl.com/nzssd-target – in summary, test for:[4]

- Fasting glucose levels when on nocte basal insulin. Check for three days before a dose change.
- Pre and two hours post glucose levels at meals with sulfonylurea or bolus/premixed insulin. Check for three days before a dose change.

References

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6. Health Navigator New Zealand. Trulicity: www.healthnavigator.org.nz/medicines/d/dulaglutide and Victoza: www.healthnavigator.org.nz/medicines/v/victoza (Accessed 28 February 2023).

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