Initiating treatment with empagliflozin in adult patients with type 2 diabetes

Algorithms,
notes and talking points

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When clinically indicated, empagliflozin can be started in adult patients with type 2 diabetes using the steps shown in this resource.

Always maintain metformin treatment if tolerated.

Talking points, relevant for all patients starting empagliflozin, are provided along with two algorithms and accompanying prescribing notes.

Which algorithm you follow will depend on your patient's level of hypoglycaemia risk.

If your adult patient with type 2 diabetes is not using a sulfonylurea or insulin they will have no significant risk of developing hypoglycaemia when starting empagliflozin. For these patients, follow Algorithm 1.

If your adult patient with type 2 diabetes is currently using a sulfonylurea or insulin they will have a risk of developing hypoglycaemia when starting empagliflozin. For these patients, follow Algorithm 2.

Note: This resource is designed for use once a decision has been made to consider treatment with empagliflozin. A similar resource has been developed for initiating dulaglutide. At the time of writing, only one of these agents can be funded on Special Authority for any one patient.

When deciding whether empagliflozin or dulaglutide would be most suitable for your patient, consider that:

- The sodium–glucose cotransporter-2 (SGLT2) inhibitor empagliflozin is typically the choice for patients in whom heart failure (particularly with reduced ejection fraction) or diabetic kidney disease predominates.
- The glucagon-like peptide 1 (GLP-1) receptor agonist dulaglutide 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.

If tolerability with the use of one of these newly funded drugs becomes an issue, the alternative option can be considered for funded use.

For further, comprehensive information, visit the New Zealand Society for the Study of Diabetes (NZSSD) at www.nzssd.org.nz

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

Talking points – empagliflozin

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

Benefits and harms

Expected benefits – in brief, empagliflozin:

- reduces systolic blood pressure by 4–5mmHg
- reduces the risk of hospitalisation for heart failure
- reduces the risk of death from heart attack (one less person in 45 people over three years)
- reduces death from all causes by 15%
- reduces the risk of progression to end-stage renal disease by about 33%
- reduces HbA1c by about 8mmol/mol, possibly more with higher baseline HbA1c
- leads to a possible 2kg weight loss.

Potential adverse effects – in brief, empagliflozin can cause:

- genital fungal infections – usually minor but patients should immediately report any genital or perineal tenderness or swelling, or fever and feeling unwell; good personal hygiene can minimise the risk
- urinary tract infections – uncommon (about 8% of patients have mild UTI)
- nausea – in about 2% of patients
- increased thirst
- increased urination – about 1 in 45 people
- euglycaemic ketoacidosis – rare, but report any nausea, vomiting, anorexia, abdominal pain, shortness of breath, sweet-smelling breath, metallic taste or general malaise.

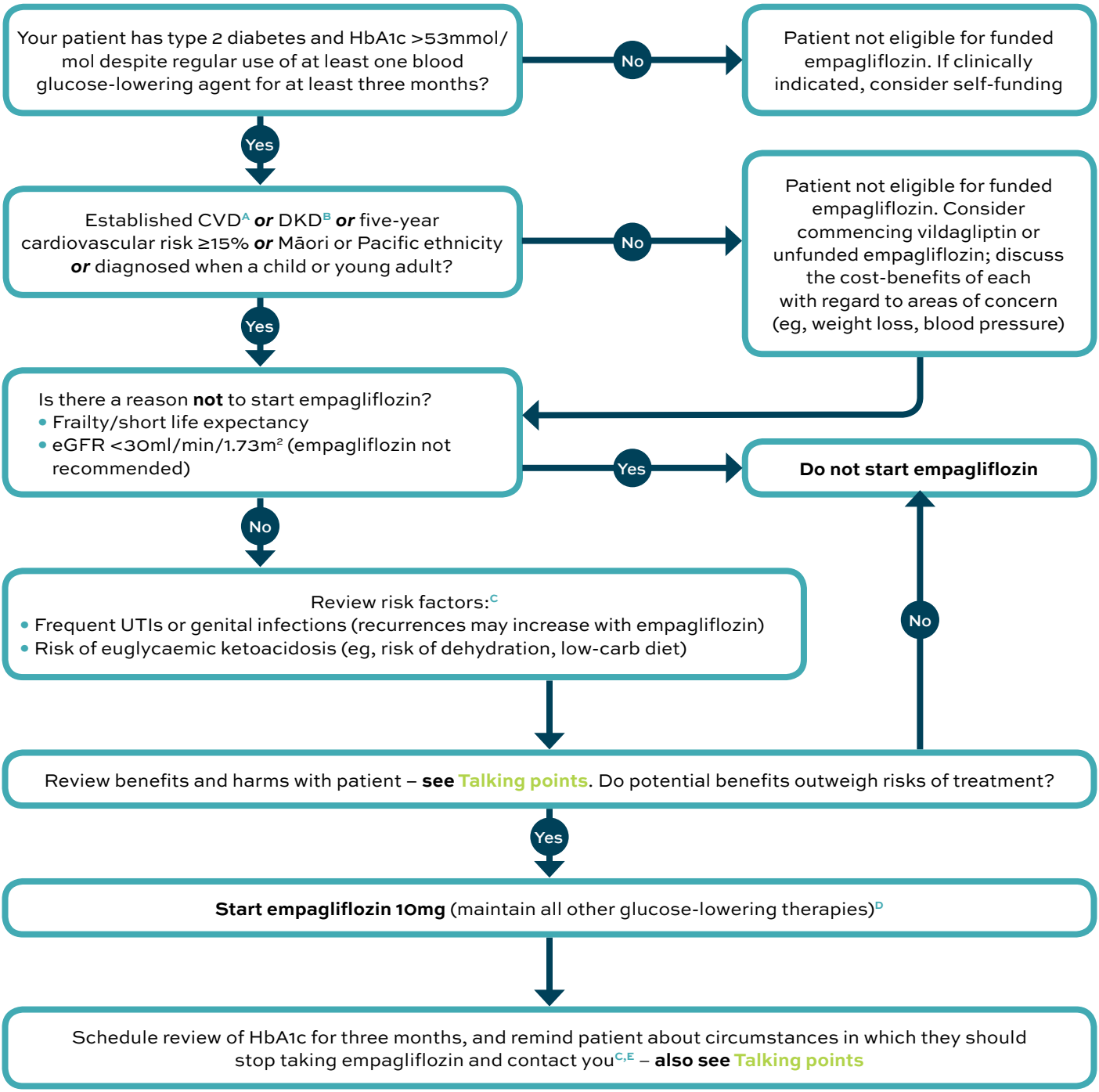
Points to raise with your patients

- Continue your other medicines unless specifically told to stop by your healthcare provider.
- Don't be surprised if you are asked to change the doses of your other blood glucose-lowering medicines over the next four weeks.
- 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) – and it is important to avoid any 'keto-diet'.*
- Remember to check your feet and maintain good foot care.
- Contact your practice if you notice any infections or rashes. Make sure to tell other healthcare professionals that you are taking empagliflozin. Stop empagliflozin at least two days before elective surgery, and four days prior to procedures that use bowel prep (eg, colonoscopy).
- **Stop empagliflozin** if you have any of the following: stomach pains, nausea, vomiting, shortness of breath, a sweet smell on the breath, a metallic taste, or feel generally very tired or confused – **and contact your healthcare provider.**

* See the 2021 *NZSSD Position Statement on Ketogenic or Very-Low-Carbohydrate Diets and the Use of SGLT2-inhibitors in Adults with Type 2 Diabetes* (scroll down to 'Education')

Algorithm 1 – empagliflozin

For type 2 diabetes patients NOT using a sulfonylurea or insulin



Algorithm 1: Additional prescribing notes

A. **Established CVD** (cardiovascular disease) is defined as: 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.

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.

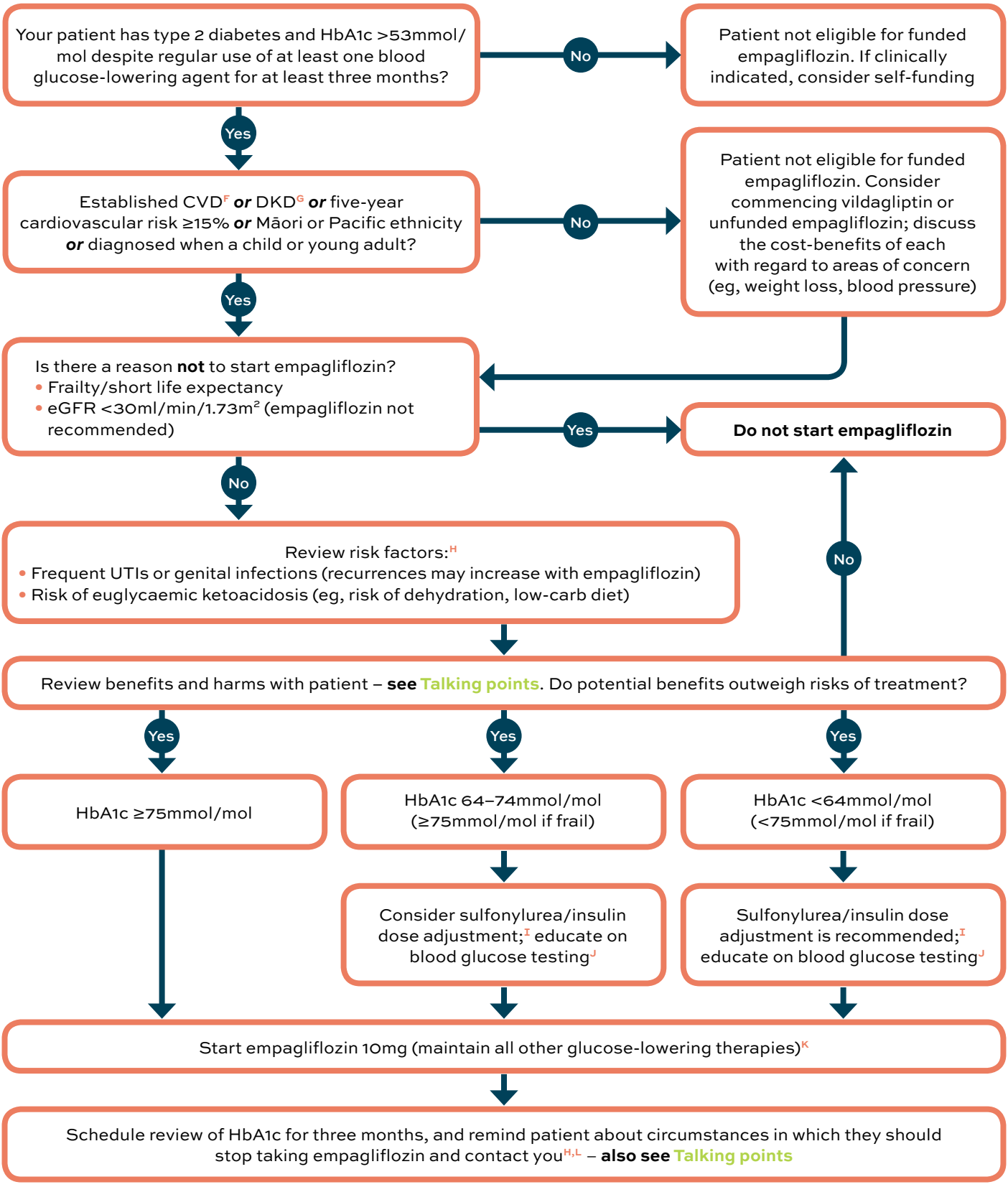
C. **Serious adverse effects to be alert for:**
- **Euglycaemic ketoacidosis.** Occurs in approximately one to eight cases per 1000 patient–years of use (usually in first six months). Risk factors include low-carb diet, volume depletion, excess alcohol consumption, serious illness/infection, surgery (including colonoscopy) and high pancreatitis risk.
  - *Monitor patient for:* Dehydration, especially in summer and with increased exercise, or with diuretic use. Symptoms of euglycaemic ketoacidosis include nausea, vomiting, anorexia, abdominal pain, shortness of breath, sweet-smelling breath, metallic taste or general malaise.
  - *Stop empagliflozin:* Immediately if there are symptoms of euglycaemic ketoacidosis. Empagliflozin should be stopped temporarily if there is prolonged fasting due to acute illness or surgery – stop two days prior to elective procedures, and four days prior to procedures using bowel prep (eg, colonoscopy).
  - *Ketone testing:* Euglycaemic ketoacidosis is due to glucose excretion in exchange for ketones, so blood ketone testing is more accurate than blood glucose testing.
- **Fournier's gangrene.** Extremely rare but may progress quickly. Monitor for pain, redness or swelling in the genital or perineal area, or fever or malaise.

D. **The starting dose of empagliflozin (Jardiance)** is 10mg daily, titrating to 25mg daily if tolerated and needed. A funded combination product (Jardiamet) is available (5mg or 12.5mg empagliflozin with 500mg or 1000mg metformin). Jardiamet is a twice-daily formulation, as opposed to once-daily monotherapy with Jardiance. Until tolerability is established, it is advisable to use separate metformin and empagliflozin preparations. Safety and efficacy in individuals who are pregnant or lactating or are younger than 18 years have not been established.

E. **The risk of hypoglycaemia is low** when a patient is not on a sulfonylurea or insulin; no dosage adjustment of other medicines is usually required when starting empagliflozin.
- **Refer to** NZ Society for the Study of Diabetes (NZSSD) Type 2 Diabetes Management Guidelines: Sick day management in patients with diabetes: tinyurl.com/nzssd-sick-day

Algorithm 2 – empagliflozin

For type 2 diabetes patients using a sulfonylurea or insulin



Algorithm 2: Additional prescribing notes

F. **Established CVD** (cardiovascular disease) is defined as: 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.

G. **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.

H. **Serious adverse effects to be alert for:**

- **Euglycaemic ketoacidosis**. Occurs in approximately one to eight cases per 1000 patient–years of use (usually in first six months). Risk factors include low-carb diet, volume depletion, excess alcohol consumption, serious illness/infection, surgery (including colonoscopy) and high pancreatitis risk.
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  - *Stop empagliflozin:* Immediately if there are symptoms of euglycaemic ketoacidosis. Empagliflozin should be stopped temporarily if there is prolonged fasting due to acute illness or surgery – stop two days prior to elective procedures, and four days prior to procedures using bowel prep (eg, colonoscopy).
  - *Ketone testing:* Euglycaemic ketoacidosis is due to glucose excretion in exchange for ketones, so blood ketone testing is more accurate than blood glucose testing.
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I. **Consider dosage adjustment of sulfonylurea and insulin based on patient's HbA1c.**

- **HbA1c <64mmol/mol (<75mmol/mol if frail):** 15–20% insulin dose reduction and 50% sulfonylurea dose reduction (or stop sulfonylurea) recommended when starting empagliflozin.
- **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 glycaemic reduction and hypoglycaemia risk.

J. **Blood glucose monitoring** is discussed in detail at tinyurl.com/nzssd-target
In summary, test for:

- 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.

K. **The starting dose for empagliflozin (Jardiance)** is 10mg daily, titrating to 25mg daily if tolerated and needed. A funded combination product (Jardiamet) is available (5mg or 12.5mg empagliflozin with 500mg or 1000mg metformin). Jardiamet is a twice-daily formulation, as opposed to once-daily monotherapy with Jardiance. Until tolerability is established, it is advisable to use separate metformin and empagliflozin preparations. Safety and efficacy in individuals who are pregnant or lactating or are younger than 18 years have not been established.

L. **Refer to** NZSSD Type 2 Diabetes Management Guidelines: Sick day management in patients with diabetes: tinyurl.com/nzssd-sick-day

Credits

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Intended users: This resource is intended to guide prescribers through the process of starting empagliflozin in adult patients with type 2 diabetes

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