Initiating treatment with empagliflozin

Algorithms,
notes and talking points

Algorithms, notes and talking points

When clinically indicated, empagliflozin can be started in 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 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 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.

Credits

Primary editor: Richard French

Contributing author: Brendan Duck

Acknowledgements: Linda Bryant, Andrea Copeland

Publication date: May 2021, Updated June 2021

Resource review date: May 2023

Resource code: HAH1018, HAH1021

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

Bibliography: Available with the online version

Published by: He Ako Hiringa with support from PHARMAC

Talking points

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

Expected 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 per cent
- reduces the risk of progression to end-stage renal disease by about 33 per cent
- 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:

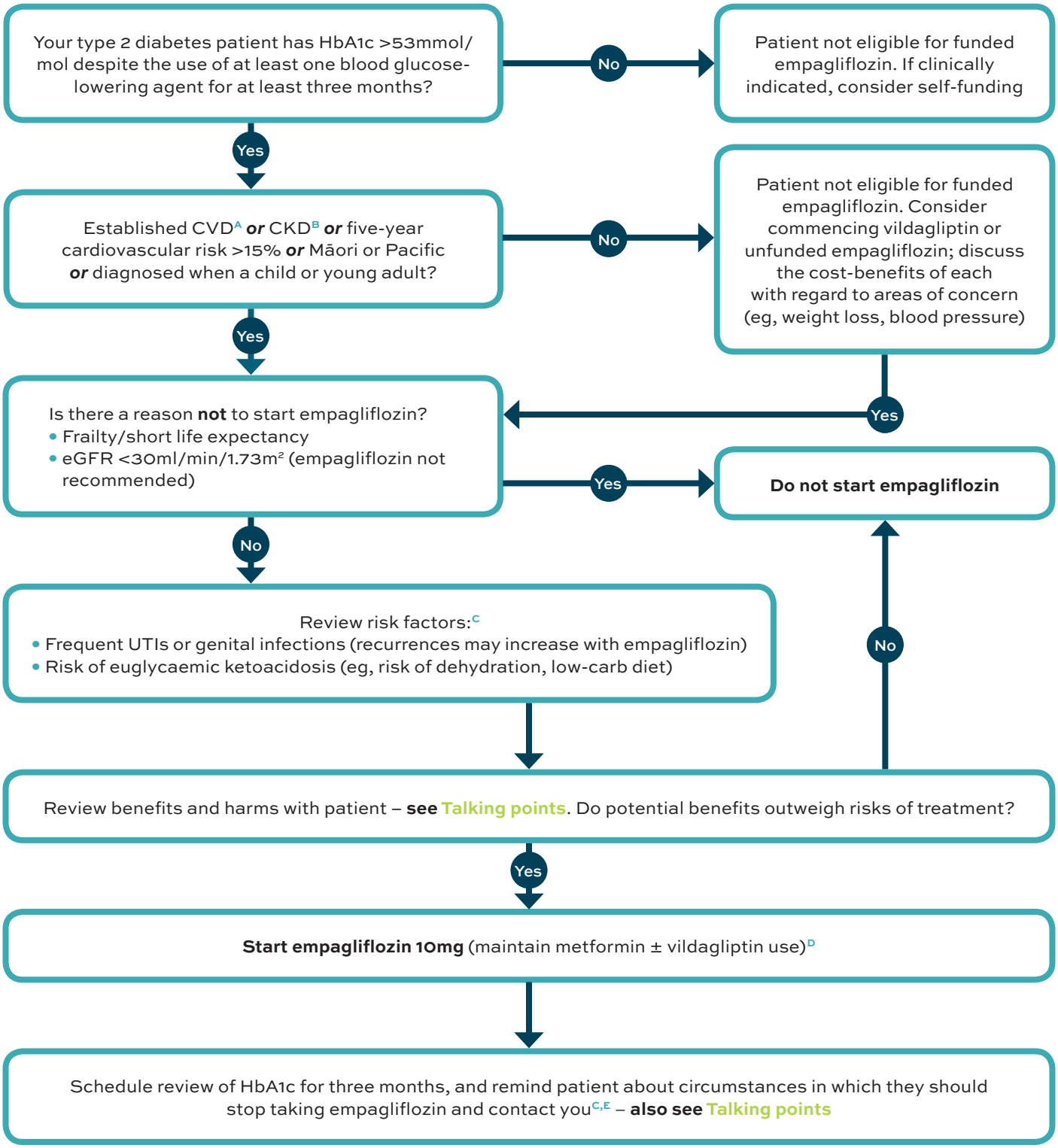
- genital fungal infections – usually minor but patients should immediately report any genital or perineal tenderness or swelling, or fever and feeling unwell; good personal hygiene can minimise the risk
- urinary tract infections – uncommon (about 8 per cent of patients have mild UTI)
- nausea – in about 2 per cent of patients
- increased thirst
- increased urination – about one person 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. When having elective surgery (including colonoscopy), it is advised to stop empagliflozin two days beforehand.
- **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.**

Algorithm 1

For type 2 diabetes patients NOT using a sulfonylurea or insulin



Algorithm 1: Additional prescribing notes

A. **Established CVD** (cardiovascular disease) is defined as a history of ischaemic heart disease, cerebrovascular disease, heart failure or peripheral vascular disease.

B. **Established CKD** (chronic kidney disease) is defined as eGFR <60ml/min/1.73m^2 or a urinary albumin–creatinine ratio >3mg/mmol.

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 (including 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.

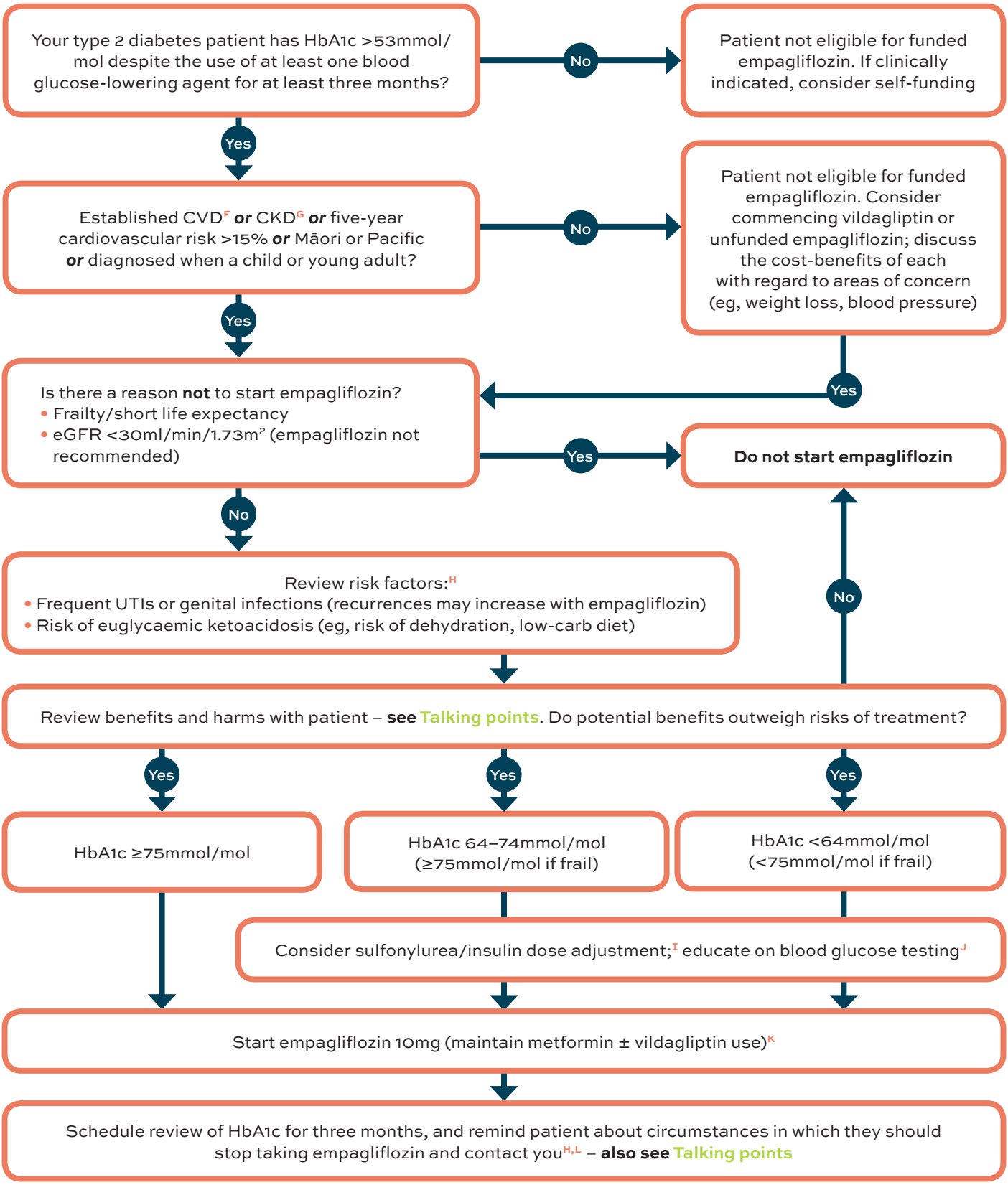
D. **The starting dose of empagliflozin (Jardiance)** is 10mg daily, titrating to 25mg daily if tolerated and needed. A funded combination product (Jardiamet) is available (5mg or 12.5mg empagliflozin with 500mg or 1000mg metformin). Jardiamet is a twice-daily formulation, as opposed to once-daily monotherapy with Jardiance. Until tolerability is established, it is advisable to use separate metformin and empagliflozin preparations.

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

For type 2 diabetes patients using a sulfonylurea or insulin



Algorithm 2: Additional prescribing notes

F. **Established CVD** (cardiovascular disease) is defined as a history of ischaemic heart disease, cerebrovascular disease, heart failure or peripheral vascular disease.

G. **Established CKD** (chronic kidney disease) is defined as eGFR <60ml/min/1.73m^2 or a urinary albumin–creatinine ratio >3mg/mmol.

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.
  - *Monitor patient for:* Dehydration, especially in summer and with increased exercise, 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 (including 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.

I. **Consider dosage adjustment of sulfonylurea and insulin based on patient's HbA1c.**

- **HbA1c <64mmol/mol (<75mmol/mol if the patient is frail):** consider 15–20% insulin dose reduction and 50% sulfonylurea dose reduction (or stop sulfonylurea) when starting empagliflozin.
- **HbA1c 64–74mmol/mol (≥75mmol/mol if the patient is 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 in the NZSSD Type 2 Diabetes Management Guidelines: Glycaemic monitoring and targets for type 2 diabetes: 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.

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