

Best Practice Message

July 2025

Empagliflozin – a reminder of the risks

Practice changing moments

- Advise patients taking empagliflozin about:
 - Risk factors, signs and symptoms of ketoacidosis.
 - Risk factors, signs and symptoms of Fournier's gangrene. Encourage patients to maintain good genital hygiene.
 - 'Sick day' guidance.
- Patients taking empagliflozin are more likely to develop ketoacidosis when additional risk factors are present, such as reduced caloric intake, severe dehydration (due to illness, infection, or surgery), pancreatic disorders, reduced insulin dose, insulin insufficiency, heavy alcohol use, or a history of ketoacidosis. This may include patients without Type 2 diabetes.
- The risk of Fournier's gangrene is increased in patients taking empagliflozin who are immunosuppressed or obese.

Background

Empagliflozin is currently the only sodium-glucose co-transporter 2 (SGLT2) inhibitor funded and available in Aotearoa. Empagliflozin has been funded in Aotearoa for type 2 diabetes management since February 2021.

While initially indicated for diabetes, the EMPEROR-REDUCED trial showed that empagliflozin reduced the risk of cardiovascular death or hospitalisation for heart failure by approximately 25%, regardless of diabetes status.¹⁻³ SGLT2 inhibitors are strongly recommended in patients with heart failure with reduced ejection fraction (HFrEF), and should be considered for use in patients with heart failure with preserved ejection fraction (HFpEF).⁴ In December 2024 Pharmac widened empagliflozin access for patients with HFrEF (with [Special Authority](#) criteria).

Empagliflozin is also indicated for chronic kidney disease (CKD). Evidence from the EMPA-KIDNEY trial showed empagliflozin reduces the risk of kidney disease progression and cardiovascular death in a broad CKD population, including patients without diabetes.⁵ This indication is not currently funded by Pharmac. SGLT2 inhibitors should be considered for CKD patients and offered as a self-funded option. Refer to [HealthPathways](#) for further guidance.

Since 2021 there have been 278 reports to the Centre for Adverse Reactions Monitoring (CARM) involving empagliflozin (or the empagliflozin + metformin combination product). Diabetic ketoacidosis and Fournier's gangrene feature frequently in these reports. Death was reported in 7 cases.⁶ Empagliflozin was listed as number one in CARM's **10 significant learnings from the NZ Centre for Adverse Reactions Monitoring (CARM) database Goodfellow presentation in 2024 by Dr Jennifer Lee and Dr Ruth Savage**. A summary of the presentation can be found [here](#) (see appendix).

Diabetic ketoacidosis (DKA)

Empagliflozin can increase the risk of diabetic ketoacidosis (DKA). In around a third of DKA cases, blood glucose levels are normal or only mildly elevated (euglycemic DKA). The mechanism involves several factors⁷:

Reduced Insulin Secretion:

↑ Ketogenesis

Ketone reabsorption in the kidney:

↑ Circulating ketones

Increased Glucagon Secretion:

↑ Glucose production, Lipolysis and Ketogenesis

Osmotic diuresis and dehydration:

↑ Glucagon, Cortisol, Adrenaline → Ketogenesis

DKA risk factors

Patients taking SGLT2 inhibitors are more likely to develop ketoacidosis when other risk factors are present including⁷⁻¹⁰.

- acute illness or infections
- surgery
- severe dehydration
- reduced caloric intake
- low carbohydrate diet (< 130g of carbohydrate per day)
- pancreatic disorders
- insulin dose reduction
- insulin insufficiency
- heavy alcohol use
- history of ketoacidosis.

Although the risk is greater in patients with Type 2 Diabetes (T2DM), there have been reports of euglycemic DKA in patients without T2DM.¹¹ Due to the risk of DKA, empagliflozin is contraindicated in patients with Type 1 Diabetes.⁹

Signs and symptoms of DKA and what to do

Patients should be advised to present to their general practice or hospital to have their ketones checked if they experience symptoms, regardless of the blood glucose level. Signs and symptoms of diabetic ketoacidosis (DKA) include^{9,12}:

- difficulty breathing
- nausea
- vomiting
- anorexia
- excessive thirst
- abdominal pain
- confusion and unusual fatigue or sleepiness
- a sweet smell to the breath
- a sweet or metallic taste in the mouth
- a different odour to urine or sweat.
- deep gasping breathing
- confusion
- coma.

If a patient presents with the above, practitioners should test blood capillary ketones (urine ketone testing may be unreliable). If capillary ketones are over 1.5 mmol/L, request [acute diabetes assessment](#).

Managing this risk - Sick day guidance

To mitigate risk, temporary discontinuation of empagliflozin during acute illness or surgery is recommended. 'Sick day' guidance, includes advising patients to pause medicines that increase the risk of AKI during acute intercurrent illness, until 48 hours after feeling better and eating and drinking normally. See patient resources below for patient handouts.

A 2022 audit of inpatients admitted to Te Matau a Māui Hawke's Bay Hospital found that 82% of patients who were taking empagliflozin prior to admission stated they had not been provided with information from a healthcare professional about sick day management.

Patients should also be advised to stop empagliflozin for at least 3 days before¹⁰:

- Any elective procedure that involves reduced oral intake for more than 12 hours, including dental surgery.
- Bowel prep for a (e.g. colonoscopy) or a low carbohydrate diet (e.g. bariatric surgery).

Fournier's gangrene

Since 2021, there have been over 30 empagliflozin-related CARM reports of Fournier's gangrene (FG), also known as necrotising fasciitis of the perineum and genitalia. Whilst this adverse effect had previously been identified, CARM noted that there appears to be an overrepresentation in Māori and Pacific people, even accounting for higher use in this group due to the Special Authority access criteria. FG can progress rapidly, with most cases reported requiring surgical debridement. FG is life threatening and fatal cases have occurred in Aotearoa.

Risk factors of FG

FG typically affects male patients, but cases have been reported in females. Diabetes itself is a common risk factor for FG. Other risk factors include^{9,13}:

- Immunosuppression
- Alcoholism
- Cirrhosis of the liver
- Systemic Lupus Erythematosus
- Crohn disease
- Human Immunodeficiency Virus (HIV) infection
- Morbid obesity
- Anecdotally Māori or Pacific patients may be more at risk.

Signs and symptoms of FG and what to do

Advise patients to seek immediate medical attention if they experience pain, tenderness, redness or swelling of the genital or perineal area, particularly with associated fever or malaise. These symptoms can worsen quickly. Discontinue empagliflozin immediately if FG is suspected.⁹ Primary care clinicians may consider requesting [acute urology assessment](#) if patients report significant pain, fevers, and redness out of keeping with mild infection.

Managing the risk

Managing the risk of genitourinary infections includes advising patient on correct hygiene:

- Women – Wash the genital area twice daily and aim to keep the area dry. Change pads regularly.
- Men – Wash the area a minimum of once daily and aim to keep the area dry. Extra care should be taken if uncircumcised to avoid scarring of prepuce, resulting in inability to retract foreskin.

Further reading and resources

- **Medsafe:**
[Empagliflozin: advise patients on the risk of ketoacidosis and Fournier's gangrene](#)
[Spotlight on empagliflozin](#)
[Reminder: Flozins and the risks of diabetic ketoacidosis and Fournier's gangrene](#)
[Reminder: risk factors for ketoacidosis with SGLT inhibitors](#)
[Jardiance datasheet](#) and [Jardiamet datasheet](#)
- **Health Hawkes Bay Best Practice Messages:**
[Managing medicines during 'sick days'](#)
[Adverse event reporting](#)
[Dulaglutide and empagliflozin treatment decision](#)
- **HealthPathways Te Matau a Māui Hawke's Bay:**
[Heart Failure](#)
- **New Zealand Formulary**
[Empagliflozin monograph](#)
[Empagliflozin + metformin monograph](#)
- **New Zealand Society for the Study of Diabetes.**
[Periprocedural DKA with SGLT2 Inhibitor Use in People with Diabetes](#)
- **Health Hawke's Bay Thalamus Dashboard**
[Diabetic on Empagliflozin/Dulaglutide](#)

Patient resources

- **Healthify has printable patient leaflets in multiple languages:**
[At home sick day advice](#)
[Empagliflozin](#)

CARM reports

Prescribers should continue to report adverse reactions to all medications to the Centre for Adverse Reactions Monitoring (CARM). This allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals can report any suspected adverse reactions via [this form](#).

SMARS disclaimer

Information about suspected adverse reactions reported to CARM was sourced from the Suspected Medicines Adverse Reaction Search (SMARS) Database (up to 31/03/2025). For a copy of the guidelines of information found on SMARS please see [here](#).

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Disclaimer: The information and advice contained in this document is based upon evidence from available resources at our disposal at the time of publication, and reflects best practice. However, this information is not a substitute for clinical judgment and individualised medical advice. Health Hawke's Bay accepts no responsibility or liability for consequences arising from use of this information.