# Perioperative management of SGLT2 inhibitors

CATAG Teaching Tool

## Introduction

SGLT2 inhibitor use requires careful consideration and management in the perioperative period. Indications for SGLT2 inhibitor use include type 2 diabetes, heart failure and chronic kidney disease.[1] SGLT2 inhibitor-associated ketoacidosis most commonly occurs in diabetic patients taking SGLT2 inhibitors;[2, 3] however, it can occur less frequently in non-diabetic patients.[4]

SGLT2 inhibitor-associated ketoacidosis may be precipitated by fasting or surgery and may occur in the presence of normal or mildly elevated blood glucose levels.[3] Ketosis can herald the development of ketoacidosis[2] and point-of-care blood ketone testing is strongly recommended to detect and monitor people who are or have been taking a SGLT2 inhibitor.[3, 4]

This case scenario can be used as a teaching tool by clinical educators in teaching sessions for medical officers, nurses, pharmacists, and students. It provides a clinical example of optimal management of people on SGLT2 inhibitors in the perioperative period and promotes individualised patient-centred care with shared decision-making and informed consent. It can be used by educators to stimulate discussion of current practice and opportunities for quality improvement.

## Case Scenario for SGLT2 inhibitors and ketone testing in the perioperative period

### Preadmission/Preassessment

Ming Wei is a 68-year-old retired male who, with prior review and approval from his endocrinologist, is undergoing a planned left knee replacement. He moved to Australia from China in 2014; he speaks limited English and accepts the use of an interpreter. He is 64kg and is 165cm tall. His medical history includes type 2 diabetes mellitus, hypertension, chronic kidney disease (stage 3a), and osteoarthritis. He has no known allergies or drug intolerances. His current medicines include:

- metformin extended release (XR) 1000mg in the morning,
- empagliflozin 10mg in the morning,
- lisinopril 20mg in the morning,
- amlodipine 5mg in the morning,
- atorvastatin 20mg in the morning and
- paracetamol modified release (MR) 1330mg three times a day.

He lives at home with his wife Lin, who speaks fluent English and is a retired nurse.

### Discussion Points

During the preadmission appointment, what instructions should Ming and his wife Lin be provided regarding Ming's upcoming admission for his left knee surgery?

Discuss perioperative management of patients taking SGLT2 inhibitors and the importance of preventing SGLT2 inhibitor-associated ketoacidosis.

**Table 1:** Ming's preadmission medicines plan

| Medicine and strength | Prescribed dose | Action and reason |
|---|---|---|
| **Metformin XR 1000mg** | 1 tablet in the morning. | **Continue** as normal.[4] |
| **Empagliflozin 10mg** | 1 tablet in the morning. | **Do not take on 6, 7, or 8 October**<br>This will not be restarted until you are eating and drinking normally after the operation.[3] |
| **Lisinopril 20mg** | 1 tablet in the morning. | **Do not take on 8 October.*** |
| **Amlodipine 5mg** | 1 tablet in the morning. | **Continue** as normal. |
| **Atorvastatin 20mg** | 1 tablet in the morning. | **Continue** as normal. |
| **Paracetamol MR 665mg** | 2 tablets three times a day. | **Continue** as normal. |

*Perioperative continuation or cessation of lisinopril remains a contentious issue, currently the United Kingdom's Handbook of perioperative medicines provides advice to omit the day of surgery. CATAG notes that the The Stop-or-Not Randomized Clinical Trial recently published data that may indicate that Renin-Angiotensin System Inhibitors could be continued. Please see here for more information.

## Admission

Ming is admitted to hospital on 8 October 2024 for elective knee replacement surgery. He has been instructed to fast from midnight before the surgery; his last meal was at 8 pm the previous night. He has followed the preadmission medicines plan discussed at his preadmission review:[3, 4, 5]

The anaesthetist confirms with Ming, via an interpreter, that he has not taken empagliflozin in the past 3 days, and did not take lisinopril that morning.

## Preoperative Assessment

Ming reports feeling well, albeit slightly anxious about the procedure and recovery.

*Overall appearance*

- *well-kept, smiling, interacting pleasantly with staff*

*Observations*

- *BP 130/80 mmHg*
- *HR 72 bpm*
- *RR 16/min*
- *Temp 36.8°C*

*Blood Glucose*

- *8.4 mmol/L (fasting)*

*HbA1c*

- *8%*

*Ketone testing*

- *Point-of-care blood ketones: 0.8mmol/L*

*eGFR*

- *50mL/min*

## Preoperative Management

### Discussion Points

When should Ming's blood glucose and ketones next be rechecked?

Discuss what actions should occur if:

- blood ketones become elevated.
- blood glucose levels become raised before SGLT2 inhibitor can be restarted (i.e. before Ming is eating and drinking normally).
- Ming becomes unwell.
- suggested activity: compare the local protocol to Periprocedural Diabetic Ketoacidosis (DKA) with SGLT2 Inhibitor Use In People with Diabetes (May 2023) - Australian Diabetes Society.

What additional factors require consideration?

If the patient failed to omit their empagliflozin, does this result in an automatic cancellation of the procedure?

Ming's preoperative assessment is reviewed by the clinical team. It is identified, with reference to the Australian Diabetes Society's Periprocedural Diabetic Ketoacidosis (DKA) with SGLT2 Inhibitor use in People with Diabetes and/or local guidance/protocol, that Ming's operation can proceed with hourly blood glucose and blood ketone testing during the procedure.[3] The clinical team, with permission from Ming, uses a translator to discuss the procedure and the monitoring plan with Ming and his wife, Lin. Ming and his wife state that they understand the risks and consent to proceed with the surgery. It is also noted and communicated that Ming will require continued blood glucose and ketone monitoring postoperatively.

Identification of the need for blood glucose and blood ketone monitoring should prompt nursing staff to calibrate the blood glucose and blood ketone meters and review the expiry dates of testing strips.

**Note:** A routine quality control process should be in place to check blood glucose and ketone meters in areas where blood glucose or ketone monitoring is conducted. Each hospital should have procedures based on the meter's manufacturer's quality control requirements.

Additionally, after reviewing the hospital's guidance/protocol (which may be local, statewide, or national), the team discusses and formulates possible management plans for Ming.

### Management plans

The following boxes outline possible management plans for Ming.

#### If Ming's Ketones elevate further

While Ming's management goals during his admission include reducing the risk of ketoacidosis, ketones are a physiological response to starvation and raised ketone levels can occur in the absence of acidosis.[3] Noting that there have been reports of ketone levels of up to 1.7mmol/L in the absence of acidosis for people with or without type 2 diabetes and not taking an SGLT2 inhibitor, the team will carefully monitor Ming's blood glucose and blood ketone levels,[3] and implement local protocols such as 'Sip Til Send'.

If Ming's blood ketone levels elevate to >1mmol/L, the team will perform a blood gas analysis to determine if Ming is in ketosis with or without metabolic acidosis. His management will be guided by the principles of ADS-ANZCA perioperative diabetes and hyperglycaemia management guidelines and likely utilise insulin and/or glucose infusion if the decision is made to continue the procedure[3, 5]

Discussion Point: Periprocedural Diabetic Ketoacidosis (DKA) with SGLT2 Inhibitor Use In People with Diabetes

Periprocedural Diabetic Ketoacidosis (DKA) with SGLT2 Inhibitor use in People with Diabetes

ADS-ANZCA perioperative diabetes and hyperglycaemia management guidelines

### If Ming's blood glucose levels rise

Ming will be prescribed insulin (as per local guidelines) to manage any elevations in blood glucose perioperatively (and postoperatively) prior to reinitiation of the SGLT2 inhibitor.[5,6]

### If Ming's condition deteriorates

If Ming becomes unwell, the team will use arterial or venous blood gases to measure the Standard Base Excess* (SBE). If his ketones persist to be >1.0mmol/L and the base excess is <-5mmol/L, it will be assumed he has diabetic ketoacidosis and that the team will liaise with the hospital's endocrinology or ICU units according to the local DKA protocol.[3,5]

Management objectives, if this occurs, would be rehydration, intravenous insulin (with added glucose infusion if the BGL is <15mmol/L) and continued hourly monitoring of blood glucose, ketones, blood gases and potassium with appropriate action to escalate or de-escalate treatment.[3,5] This would be accompanied by a review by an endocrinologist or physician on-call and critical care specialists.[3,5]

*Note: pH, bicarbonate and anion gap ranges also inform diagnosis and management of DKA. Please refer to your local DKA guidelines.

### Additional consideration

If Ming had not omitted empagliflozin for 3 days, the surgical team, in consultation with the anaesthetist, would review the patient's individual circumstances and consider the urgency of the procedure, his comorbidities, surgical factors, HbA1c, blood ketones, and base-excess to determine the best course of action.[3]

## Postoperative Management

After an uneventful procedure, Ming is sent to the ward (via recovery) with instructions to continue VTE prophylaxis[7] as per local guidelines and for 2-hourly blood glucose and blood ketone testing to be conducted initially and adjusted as clinically directed to enable the patient to rest overnight. Monitoring continues during his recovery. It is noted in the progress notes that Ming's lisinopril can be restarted on the morning of the 9 October and the SGLT2 inhibitor should be withheld until he is eating and drinking normally.[3,5] Ming's expected discharge date is 10 October.

Ming's blood glucose levels and ketones remain within acceptable limits during his recovery, and his eGFR remains stable at his baseline eGFR of 50mL/min. Unfortunately, during his recovery, Ming complains to his wife, Lin, about the 'hospital food' and his nurses note he hasn't eaten his meals. Despite this, he is generally well. Since empagliflozin should not be restarted until he is eating and drinking normally, it is decided within the multidisciplinary team that with support from his wife, Ming's empagliflozin should be restarted post-discharge. Patient and carer communication (both written and verbal via the translator), and GP communication will be necessary.

### Discussion Points

What should be included in Ming's discharge communications?

What additional services could Ming benefit from?

What strategies and/or hospital resources could you use to support effective communication with culturally and linguistically diverse people?

Does your hospital have a standardised pain management discharge plan?

- Recommended learning: MAIA: Preventing progression to persistent pain teaching tool.

MAIA: Preventing progression to persistent pain teaching tool

## Discharge Planning

Ming's multidisciplinary team consist of the orthopaedic surgeon, junior medical officer, pharmacist, nurse, physiotherapist, diabetes educator and dietitian and collaboratively they develop a discharge plan, which ensures all aspects of his care upon returning home is communicated with the appropriate supporting documentation. After gaining permission from Ming, the team coordinates with the hospital translation services and Ming's wife to ensure effective discharge counselling is provided. In addition to this, the junior medical officer calls Ming's GP to provide a clinical handover over the phone.[6]

**Note:** Discharge planning and counselling should be prioritised to the needs of the patient and the resources available. Many discharge documents and fact sheets will not be available in other languages, however, including these resources in the discharge documentation, will assist English-speaking family members to support the patient and facilitate their recovery and rehabilitation at home.

## Day of Discharge

Upon arrival of the translator on 10 October, Ming and Lin are provided with counselling that is supported with written documentation and a comprehensive discharge summary. Included in the counselling and discharge summary are:

- provision of a SGLT2 inhibitors patient information leaflet which includes signs and symptoms of SGLT2 inhibitor-associated ketoacidosis.[8]
- provision of a sick day action plan that advises temporary metformin, empagliflozin, and lisinopril discontinuation and advice to seek medical attention in the event of acute illness or dehydration.[8, 9]
- information about Ming's follow-up appointments with the orthopaedic surgeon.
- wound care instructions emphasising the importance of optimal glycaemic control to decrease the risk of infection.[5]
- his rehabilitation plan including exercise routines and referral to a 6-week rehabilitation program.
- ongoing monitoring and management requirements:
    - Ming and Lin to seek GP review within one week for medical review and ongoing diabetes optimisation.
    - Ming and Lin to measure his blood sugar levels at home daily.[8]
- eGFR results.[6]
- education about optimal nutrition.
- a recommendation for referral to a community diabetes educator for guidance on optimising diabetes management.
- a recommendation for referral to a community dietitian for diabetes nutritional advice.
- a complete and current medicines list (see below) including information and instructions about:
    - rivaroxaban use for venous thromboembolism prophylaxis.[7]
    - paracetamol and oxycodone use for analgesia (ideally supported by a pain medicine discharge plan).
    - empagliflozin being withheld due to fasting and surgery, and when it is to restart.[6]

Patient information leaflet

Sick day action plan

**Table 2:** Instructions provided to Ming regarding his medicines

| Medicine and strength | Prescribed dose | Action and reason |
|---|---|---|
| **Rivaroxaban 10mg** | 1 tablet in the morning for 12 more days with food. | **New medicine** to prevent blood clots (venous thromboembolism prophylaxis).<br>**Stop on 21/10/2024.** |
| **Metformin XR 1000mg** | 1 tablet in the morning. | **Continued** at same dose. |
| **Lisinopril 20mg** | 1 tablet in the morning. | **Continued** at same dose. |
| **Amlodipine 5mg** | 1 tablet in the morning. | **Continued** at same dose. |
| **Empagliflozin 10mg**<br>**Stopped on the 6/10/2024 due to fasting and surgery.** | 1 tablet in the morning. | **Restart when Ming is eating and drinking normally.**<br>Monitor blood glucose levels daily and follow instructions on the SGLT2 inhibitors patient information leaflet.<br>Please note the empagliflozin restart date here: __/__/__ and tell your GP at your next visit. |
| **Paracetamol MR 665mg** | 2 tablets three times a day.<br>**Maximum of 6 tablets a day.** | **Temporary medicine for pain.**<br>You will probably need this medicine for 1 to 2 weeks. |
| **Oxycodone Immediate Release (IR) 5mg** | 1 to 2 tablets up to four times a day **if needed.**<br>**Maximum 8 tablets a day.** | **Temporary medicine for pain.**<br>You will probably need this medicine for 1 to 2 weeks. |
| If you are unwell or dehydrated, immediately contact your doctor. You may need to use your sick day action plan. | | |

## Follow-up

### Hospital Clinical Team

A member of the clinical team contacts Ming 2 days after discharge to see how he is progressing. Lin translates for Ming and informs them that he is doing well, and his appetite returned the day after discharge, so they restarted his empagliflozin. It was also confirmed that Ming had a GP appointment booked for 17 October.

### GP

Ming sees his GP 7 days after discharge for a follow-up review. Lin informs the GP that Ming restarted his empagliflozin on 11 October and that they checked his blood glucose levels daily; these have remained stable and within acceptable ranges between 6 and 8mmol/L. The GP advises Ming that he can decrease to second daily blood glucose monitoring. The GP notes his wound looks good. Ming reports his pain is decreasing and he is only taking one oxycodone IR tablet before going to the physiotherapist's rehabilitation session and at night. The GP writes Ming a script for 10 additional tablets of oxycodone IR and asks to see Ming again in one week. The GP also refers Ming to a diabetes educator, dietitian and accredited pharmacist for a comprehensive medicines review.

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