



Safety Notice 005/18

15 March 2018

Distributed to:

- Chief Executives
- Directors of Clinical Governance
- Director Regulation & Compliance Unit

Action required by:

- Chief Executives
- Directors of Clinical Governance

We recommend you also inform:

- Directors of Medical Services
- Directors of Nursing and Midwifery
- Directors of Pharmacy
- Theatre Managers
- Directors of Anaesthetics
- Directors of Emergency Departments
- Directors of Intensive Care

Expert Reference Group

Content reviewed by:

- ACI Anaesthesia Perioperative Care Network
- ACI Surgical Services Taskforce
- ACI Endocrine Network

Clinical Excellence Commission

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Review date

March 2019

Peri-operative risk of SGLT2 inhibitor–associated ketoacidosis

Background

There have been reports of patients with diabetes who are taking SGLT2 inhibitors developing euglycaemic diabetic ketoacidosis (DKA) leading to severe acidosis requiring intensive care/ high dependency unit admission during the peri-operative period¹.

Euglycaemic DKA is associated with **normal or only mildly elevated blood glucose levels** increasing the risk of a missed diagnosis and delays in management of the ketoacidosis². Ketoacidosis can be life threatening if not treated appropriately.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are oral medicines used in the management of Type 2 diabetes. The two SGLT2 inhibitors currently available in Australia are dapagliflozin and empagliflozin, available as single ingredient products or in combination with metformin. The trade names of these products are:

- *Forxiga* (contains dapagliflozin)
- *Xigduo XR* (contains dapagliflozin and metformin, controlled release preparation)
- *Jardiance* (contains empagliflozin)
- *Jardiamet* (contains empagliflozin and metformin)³.

These medicines work by reducing glucose reabsorption in the kidney (and increasing its excretion in the urine)². Usage of these agents is increasing in NSW public hospitals.

Perioperative risk

The possible triggers for euglycaemic DKA include:

- restricted dietary intake (e.g. fasted)
- surgery
- dehydration
- active infection.

Patients taking a SGLT2 inhibitor should be assessed for their risk of DKA before surgical procedures and other potentially stressful situations². Perioperative risks include dehydration, urinary tract infections and renal impairment².

References

1. [Australian Diabetes Society Alert: Severe Euglycaemic Ketoacidosis with SGLT2 Inhibitor Use in the Perioperative Period](#) 14 Feb 2018
2. [Meyer EJ, Gabb G and Jesudason D. Diabetes Care. 2018 Feb 13. doi: 10.2337/dc17-1721](#)
3. Australian Medicines Handbook 2018 (online). Adelaide: Australian Medicines Handbook Pty Ltd; 2018 January.
4. Forxiga Full Product Information, Astra Zeneca, Feb 2017 (accessed through [CIAP](#), 7 Mar 2018)

Suggested actions by Local Health Districts/Networks

1. Forward information to relevant clinicians, clinical departments/units, and Drug and Therapeutics Committees (or similar) for action.
2. Conduct a local risk assessment on the use of SGLT2 inhibitors and awareness of associated euglycaemic DKA and implement strategies to reduce risk of patient harm.
 - Strategies could include amending protocols regarding medicines to temporarily cease prior to surgery and education about the risk of missed diagnosis of DKA.
 - Detailed advice on managing the risk of SGLT2 inhibitor–associated ketoacidosis is available from:
 - [Australian and New Zealand College of Anaesthetists \(ANZCA\) Safety Alert](#)
 - [Australian Diabetes Society Alert](#)
 - Monitor blood ketone and glucose levels regularly in the pre- and post-operative period.
 - Patients who use SGLT2 inhibitors who present with symptoms such as nausea, vomiting, abdominal pain, malaise and shortness of breath, should be assessed for ketoacidosis, even if blood glucose levels are below 14 mmol/L⁴.
3. Monitor and document adverse outcomes associated with the use of SGLT2 inhibitors
4. Ensure a system is in place to document actions taken.