HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

SGLT2 inhibitors – Updated advice on monitoring ketone bodies in patients hospitalised for major surgical procedures or acute serious medical illnesses

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded its review of the risk of diabetic ketoacidosis (DKA) associated with sodium-glucose co-transporter 2 (SGLT2) inhibitors* in patients undergoing surgical procedures. SGLT2 inhibitors are indicated in adults for the treatment of Type 2 diabetes, as monotherapy or in combination with other diabetes medicines.

In 2016, following a review of the safety data available at the time, the PRAC considered that a small excess risk of DKA associated with SGLT2 inhibitors could not be excluded and that DKA with an atypical presentation may occur. The product information for SGLT2 inhibitors was updated thereafter to reflect this information and advise healthcare professionals that treatment with SGLT2 inhibitors should be interrupted in patients who are hospitalised for major surgery or acute serious illnesses due to the risk of DKA. This information was highlighted in the HPRA's Drug Safety Newsletter at that time (75th edition).

In early 2019, newly identified cases of DKA associated with SGLT2 inhibitors occurring in patients undergoing surgical procedures prompted further evaluation of the associated risk factors. Following an in-depth review of the available safety data, PRAC recommended that the Summary of Product Characteristics (SmPC) for SGLT2 inhibitors be updated to include a recommendation on how to assess for ketoacidosis in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. The updated warning recommends that ketones be monitored following interruption of SGLT2 inhibitor treatment in these patients. Treatment may be restarted when ketone values are normal and the patient's condition has stabilised. There is evidence that SGLT2 inhibitors may diminish the excretion of ketone bodies in the urine, thereby making urine measurement of ketone bodies less reliable compared to blood testing. Therefore, measurement of blood ketone levels is preferred to urine.

Advice to Healthcare Professionals

- In addition to the interruption of SGLT2 treatment in patients who are hospitalised for major surgical procedures or acute serious medical illnesses, ketone bodies should be monitored in these patients.
- Measurement of blood ketone levels is preferred to measurement of ketone bodies in the urine.
- Treatment may be restarted when the ketone values are normal and the patient's condition has stabilised.

Key Message

- Cases of DKA have been reported in patients using SGLT2 inhibitors undergoing surgical procedures.
- SGLT2 treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. Ketone bodies should be monitored in these patients, preferably by measurement of blood ketone levels.
- Treatment may be restarted when the ketone values are normal and the patient's condition has stabilised.
- The Summary of Product Characteristics (SmPC) for SGLT2 inhibitors will be updated to include a recommendation on how to assess for ketoacidosis in patients who are hospitalised for major surgical procedures or acute serious medical illnesses.
- All reports of suspected adverse reactions should be reported to the HPRA via the available methods (www.hpra.ie).

**SGLT2 inhibitor-containing products include Ebymect, Edistride, Forxiga, Qtern, Xigduo, Glyxambi, Jardiance, Synjardy, Segluromet, Steglatro, Steglujan, Invokana and Vokanamet. Further details are available on www.hpra.ie and www.ema.europa.eu.*

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