
EMA confirms recommendations to minimise ketoacidosis risk with SGLT2 inhibitors for diabetes

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Information on SGLT2 inhibitors

- Sodium-glucose co-transporter-2 (SGLT2) inhibitors are medicines used to treat type 2 diabetes. They block a protein in the kidneys called SGLT2, which absorbs glucose back from the urine into the bloodstream as the blood is filtered in the kidneys. Through this action SGLT2 inhibitors cause more glucose to be removed through the urine, thereby reducing the levels of glucose in the blood.
- In Malta SGLT2 inhibitors are authorised through the centralised procedure (See Safety Circular [P19/2015](#) for more information)

Healthcare professionals should be aware of possible atypical cases

- Diabetic ketoacidosis is a serious complication of diabetes caused by low insulin levels. Cases of diabetic ketoacidosis which were life-threatening ones and atypical have occurred in patients taking SGLT2 inhibitors for type 2 diabetes.
- Following a review of the cases, the EMA has recommended updating the product information of SGLT2 inhibitors to list diabetic ketoacidosis as a rare adverse reaction (affecting up to 1 in 1,000 patients)
- The benefits of these medicines continue to outweigh the risks in the treatment of type 2 diabetes. Healthcare professionals should exercise caution with SGLT2 inhibitors in patients with predisposing risk factors for diabetic ketoacidosis and be aware of possible atypical case presentation.

For more information about ketoacidosis risk with SGLT2 inhibitors for diabetes readers are encouraged to refer to safety circulars [P19/2015](#) and [P03/2016](#)

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In Malta

For Healthcare Professionals

Rare cases of diabetic ketoacidosis, including life-threatening ones, have occurred in patients taking SGLT2 inhibitors, used to treat type 2 diabetes. A number of these cases were atypical with patients having only moderately raised blood sugar levels and some of them occurred during off-label use and clinical trials in patients with type 1 diabetes. Therefore the EMA recommends to HCPs:

- Always consider the possibility of diabetic ketoacidosis in patients taking SGLT2 inhibitors who have non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness.
- Inform patients of the signs and symptoms of diabetic ketoacidosis and advise them to seek medical advice immediately if they develop signs and symptoms mentioned above.
- Stop treatment with SGLT2 inhibitors immediately if diabetic ketoacidosis is suspected or confirmed, and do not re-start treatment unless another clear precipitating factor for the condition is identified and resolved.
- Stop treatment with SGLT2 inhibitors temporarily in patients undergoing major surgical procedures or hospitalised due to acute serious medical illnesses. Treatment may be restarted once the patient's condition has stabilised.
- Exercise caution in patients with risk factors for ketoacidosis and inform patients of these factors. These include low reserve of insulin-secreting cells, a sudden reduction in insulin dose, an increased requirement for insulin (due to illness, surgery or alcohol abuse) and conditions that restrict food intake or can lead to severe dehydration.
- Healthcare professionals are reminded that SGLT2 inhibitors are only authorised for treating type II diabetes.

Healthcare Professionals are encouraged to refer to product information which will be updated in due course when prescribing SGLT2 inhibitor containing medicinal products for type 2 diabetes. Such information can be accessed from the Medicines Authority's website by searching for the product in the [online database](#).

Advice for patients

Rare cases of diabetic ketoacidosis have occurred in people with type 2 diabetes taking diabetes medicines known as SGLT2 inhibitors (e.g Forxiga, Invokana, Jardiance, Synjardy, Vokanamet and Xigduo). Patients should be aware that:

- Diabetic ketoacidosis is a serious complication of diabetes. Symptoms include rapid weight loss, nausea or vomiting, stomach pain, excessive thirst, fast and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to the breath, a sweet or metallic taste in the mouth, or a different odour to urine or sweat.
- If patient have any of the symptoms above while taking an SGLT2 inhibitor, contact a doctor or the nearest hospital straightaway even if their sugar level is not particularly high. Patients may need emergency treatment and their diabetes medicine may need to be changed.
- Some of the cases of diabetic ketoacidosis in people taking SGLT2 inhibitors did not show the very high sugar levels normally associated with this condition.
- Patients are encourage to refer to the Patient information leaflet found in every box of SGLT2 inhibitor medicine for diabetes

For more information on the confirmed recommendation to minimise ketoacidosis risk with SGLT2 inhibitors for diabetes please refer to the European Medicines Agency's [press release](#).

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on SGLT2 inhibitor containing medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending to <http://www.medicinesauthority.gov.mt/adrportal> or online at <http://www.medicinesauthority.gov.mt/adrportal> or to the marketing authorisation holder or their local representatives.

Prof. John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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