



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## SGLT2 inhibitors: PRAC makes recommendations to minimise risk of diabetic ketoacidosis

Healthcare professionals should be aware of possible atypical cases

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has finalised a review of SGLT2 inhibitors (a class of type 2 diabetes medicines) and has made recommendations to minimise the risk of diabetic ketoacidosis.

Diabetic ketoacidosis is a serious complication of diabetes caused by low insulin levels. Rare cases of this condition, including life-threatening ones, have occurred in patients taking SGLT2 inhibitors for type 2 diabetes and a number of these cases have been atypical, with patients not having blood sugar levels as high as expected.

An atypical presentation of diabetic ketoacidosis can delay diagnosis and treatment. Healthcare professionals should therefore consider the possibility of ketoacidosis in patients taking SGLT2 inhibitors who have symptoms consistent with the condition even if blood sugar levels are not high.

There are currently three SGLT2 inhibitors authorised in the EU (canagliflozin, dapagliflozin and empagliflozin) and they are available (alone or in combination with metformin) under the following tradenames: Ebymect, Edistride, Forxiga, Invokana, Jardiance, Synjardy, Vokanamet and Xigduo.

Patients taking any of these medicines should be aware of the symptoms of diabetic ketoacidosis, including 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.

Patients should contact their healthcare professional if they have any of these symptoms.

If diabetic ketoacidosis is suspected or confirmed, treatment should be stopped immediately and should not be re-started unless another cause for the ketoacidosis is identified and resolved.

Healthcare professionals should exercise caution in patients with risk factors for ketoacidosis and inform patients of the risk factors. These include low reserve of insulin-secreting cells, conditions that restrict food intake or can lead to severe dehydration, a sudden reduction in insulin or an increased requirement for insulin due to illness, surgery or alcohol abuse.

In addition, the PRAC recommended temporarily stopping SGLT2-inhibitor treatment in patients in hospital for major surgical procedures or due to serious illness.



The benefits of SGLT2 inhibitors continue to outweigh their risks in the treatment of type 2 diabetes. The PRAC reminds healthcare professionals that these medicines are not authorised for treating type 1 diabetes, noting that some cases of ketoacidosis had occurred with off-label use.

The PRAC's recommendations will now be forwarded to the Committee for Medicinal Products for Human Use (CHMP) for the adoption of EMA's final opinion. Further details will be published at the time of the CHMP opinion.

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### **More about the medicine**

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. By blocking the action of SGLT2, these medicines cause more glucose to be removed through the urine, thereby reducing the levels of glucose in the blood.

The following SGLT2 inhibitors are authorised in the EU: Ebymect (dapagliflozin/metformin), Edistride (dapagliflozin), Forxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Synjardy (empagliflozin/ metformin), Vokanamet (canagliflozin/metformin) and Xigduo (dapagliflozin/ metformin).

### **More about the procedure**

The review of SGLT2 inhibitors has been initiated at the request of European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's final opinion.

The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.

### **Contact our press officer**

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