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Review of diabetes medicines called SGLT2 inhibitors started

Risk of diabetic ketoacidosis to be examined

The European Medicines Agency (EMA) has started a review of canagliflozin, dapagliflozin and empagliflozin, which are medicines known as SGLT2 inhibitors used to treat type 2 diabetes. The aim of the review is to evaluate the risk of diabetic ketoacidosis, a serious condition that usually develops in people with type 1 diabetes when insulin levels are too low.

The review of SGLT2 inhibitors has been requested by the European Commission following reports[1] of diabetic ketoacidosis in patients on SGLT2 inhibitor treatment for type 2 diabetes. All cases were serious and some required hospitalisation. Although diabetic ketoacidosis is usually accompanied by high blood sugar levels, in a number of these reports blood sugar levels were only moderately increased. These uncharacteristic blood levels could delay diagnosis and treatment.

EMA will now review all available data on the risk of diabetic ketoacidosis with SGLT2 inhibitors and consider whether any changes are needed in the way these medicines are used in the EU.

While the review is ongoing, healthcare professionals will be informed in writing of the risk of diabetic ketoacidosis and how to manage it. Patients who have any concerns about their diabetes medicines should consult their doctor or pharmacist. It is important that patients with diabetes continue to take their prescribed treatment and do not stop treatment without first discussing with a healthcare professional.

More about the medicines

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.

[1] A total of 101 cases of diabetic ketoacidosis in patients treated with SGLT2 inhibitors for type 2 diabetes had been reported worldwide in EudraVigilance as of 19 May 2015. It is estimated that the exposure to these medicines is over half a million patient-years. One patient-year is equivalent to 1 patient taking the medicine for 1 year.

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Medicines containing SGLT2 inhibitors are authorised in the EU under the following trade names: Forxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin), Synjardy (empagliflozin/metformin), Vokanamet (canagliflozin/metformin) and Xigduo (dapagliflozin/metformin).

More about the risk

Diabetic ketoacidosis occurs when the body is unable to use blood glucose because insulin levels are too low. Instead, it breaks down fat as an alternative source of energy and causes a build-up of excess ketones as a by-product. Diabetic ketoacidosis is a known condition that mainly occurs in people with type 1 diabetes, but it can also be a complication of type 2 diabetes. Symptoms of diabetic ketoacidosis include difficulty breathing, confusion, feeling very thirsty, vomiting, abdominal pain, nausea, loss of appetite and unusual tiredness. Patients who develop any such symptoms should seek urgent medical attention and should be evaluated by their doctor for diabetic ketoacidosis irrespective of their blood glucose levels.

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 is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. The PRAC recommendations will then be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt a 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.