Review of diabetes medicines SGLT2 inhibitors and risk of diabetic ketoacidosis

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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.
- 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.
- In Malta the following products are authorised through centralised procedure

Active Ingredients	Product Name	Pharmaceutical Form	Classification	Authorisation Numbers	MAH/license holder
Dapagliflozin	Forxiga	Film coated tablets	POM	EU/1/12/795/001-010	AstraZeneca AB
Dapagliflozin / Metformin	Xigduo	Film coated tablets	POM	EU/1/13/900/001-012	Bristol-Myers Squibb/ AstraZeneca EEIG
Canagliflozin	Invokana	Film-coated tablets	POM	EU/1/13/884/001-008	Janssen-Cilag International N.V.
Canagliflozin / Metformin	Vokanamet	Film-coated tablets	POM	EU/1/14/918/001-012	Janssen-Cilag International N.V.
Empagliflozin	Jardiance	Film-coated tablets	POM	EU/1/14/930/001-018	Boehringer Ingelheim International GmbH
Empagliflozin / Metformin	Synjardy	Film-coated tablets	POM	EU/1/15/1003/001-040	Boehringer Ingelheim GmbH

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Information from European Medicines Agency about SGLT2 inhibitors and the risk of diabetic ketoacidosis

The European Medicines Agency (EMA) has started a review of the SGLT2 inhibitor class (canagliflozin, dapagliflozin and empagliflozin) with the aim of evaluating the risk of diabetic ketoacidosis.

- Diabetic ketoacidos is a serious condition that usually develops when the body is unable to use blood glucose as source of energy 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. This mainly occurs in people with type I diabetes however it can also be a complication of type 2 diabetes.

- There have been reports of diabetic ketoacidosis in patients on SGLT2 inhibitor treatment for type 2 diabetes.

- Diabetic ketoacidosis is usually accompanied by high blood sugar levels but in a number of these reports blood sugar levels were only moderately increased and such uncharacteristic blood sugar levels could delay diagnosis and treatment.

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's recommendation will then be forwarded to the Committee for Human Medicinal Products (CHMP) and the European Commission for a legally binding decision in due course

In Malta

For Healthcare Professionals

Healthcare Professionals are encouraged to remain vigilant for symptoms of diabetic ketoacidosis (listed below) in their patients and to refer to product information 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.

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Advice for patients

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 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. Patients who have any concerns about their diabetes medicines should consult their doctor or pharmacist.

For more information on the risk of diabetic ketoacidosis and SGLT2 inhibitors 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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