

SGLT2 inhibitors: PRAC makes recommendations to minimise 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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PRAC recommends that healthcare professionals should be aware of possible atypical cases of diabetic ketoacidosis with SGLT2 inhibitors

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

- Diabetic ketoacidosis is a serious complication of diabetes and cases of this condition have occurred rarely in patients taking SGLT2 inhibitors for type 2 diabetes. 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 and 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.
- The PRAC recommended temporarily stopping SGLT2-inhibitor treatment in patients in hospital for major surgical procedures or due to serious illness and also reminds healthcare professionals that these medicines are not authorised for treating type 1 diabetes since some cases of ketoacidosis had occurred with off-label use.
- The benefits of SGLT2 inhibitors continue to outweigh their risks in the treatment of type 2 diabetes.

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.

In Malta

For Healthcare Professionals

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.

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For Patients

Patients taking any SGLT2 inhibitors should be aware of the symptoms of diabetic ketoacidosis.

These 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
- A different odour to urine or sweat

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

For more information on PRAC's recommendations to minimise risk of diabetic ketoacidosis with 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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