

## **Prescribing of Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2 inhibitors) and risk of Diabetic Ketoacidosis (including in patients with COVID-19).**

### **Background**

#### **COVID-19, DKA and SGLT2 inhibitors**

Patients admitted with diabetes and COVID-19 infection appear to have a greater risk of hyperglycaemia with ketones, including people with type 2 diabetes and people with newly diagnosed diabetes.<sup>1</sup> **The risk is even greater if the patient is on a SGLT2 inhibitor.**<sup>1</sup> The class of SGLT2 Inhibitors includes the following drugs; Dapagliflozin, Empagliflozin, Ertugliflozin, and Canagliflozin.

COVID-19 disease precipitates atypical presentations of diabetes emergencies (e.g. mixed Diabetes ketoacidosis (DKA) and hyperosmolar states).<sup>1,2</sup> These are extremely complex to treat.

#### **MHRA Drug Safety Update 2016: SGLT2 inhibitors and risk of DKA<sup>3</sup>**

Patients taking SGLT2 inhibitors should be informed of the **signs and symptoms of DKA** and advised to seek medical advice if they develop any of these.<sup>3</sup>

Blood ketone levels should be tested in patients with ketoacidosis symptoms, even if plasma glucose is near normal.<sup>3</sup> SGLT2 inhibitors should be discontinued immediately if DKA is suspected or diagnosed.<sup>3</sup> DKA requires urgent hospital admission.

#### **MHRA Drug Safety Update 2020<sup>4</sup>**

Diabetic ketoacidosis, including euglycaemic diabetic ketoacidosis, is a rare but significant risk for the SGLT2 inhibitor class of medicines.

The MHRA have advised that SGLT2 inhibitor treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses and ketone levels measured, preferably in blood rather than urine. Treatment may be restarted when the ketone values are normal and the patient's condition has stabilised.

***All patients currently taking a SGLT2 inhibitor (either as a sole agent or in a combination product) should be reviewed and actioned as below. Please liaise with your Clinical Pharmacist / Technician for support with this.***

### **Patients with Type 1 diabetes**

In December 2021, the authorisation holder for dapagliflozin withdrew the indication for type 1 diabetes mellitus. The removal of the type 1 diabetes indication is not due to any new safety concerns and the other indications of dapagliflozin are unchanged.<sup>5</sup> Dapagliflozin was the only SGLT2 inhibitor licensed for type 1 diabetes.

Dapagliflozin was indicated in adults for the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin in patients with BMI  $\geq 27$  kg/m<sup>2</sup>, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy.<sup>5</sup>

Diabetes teams should **discontinue** the use of dapagliflozin in people with type 1 diabetes as this is a very high-risk group of people susceptible to DKA (diabetic ketoacidosis is a known risk with use of dapagliflozin in all patients with diabetes, but it occurs more frequently in patients with type 1 diabetes than those with type 2 diabetes).<sup>2,5</sup>

***Existing patients with type 1 diabetes should be identified and in liaison with the initiating prescriber, reviewed and advised to discontinue dapagliflozin, with a clear rationale provided.<sup>2,5</sup>***

Discontinuation is likely to cause a rise in their glucose levels and so patients will be advised to closely monitor their blood glucose and adjust their insulin doses accordingly.

## **Patients with Type 2 Diabetes**

SGLT2 inhibitors for type 2 diabetes have a **GREEN** traffic light classification on the Barnsley Joint Formulary.<sup>6</sup>

Patients with Type 2 Diabetes currently prescribed a SGLT2 inhibitor should **continue to take these if well but should be advised to stop taking them immediately if they become unwell (e.g. coronavirus symptoms, vomiting, diarrhoea, fever)**. This is because it may predispose them to diabetic ketoacidosis / euglycaemic DKA. A ketone and blood sugar check should take place where possible and the patient should be advised to contact their healthcare team.

Note that it is **not** necessary for all patients on SGLT2 inhibitors to be given the ability to monitor their capillary blood glucose unless they are prescribed an additional medication which requires this. Patients prescribed SGLT2 inhibitors would not usually be issued with a ketone testing meter (unless identified as high risk of recurrent diabetic ketoacidosis by the diabetes specialist team). Their ketone levels should be checked if they present as unwell in line with sick day guidance, using a practice meter, even if their blood glucose is in the normal range.<sup>7</sup>

***Patients with type 2 diabetes should be reminded/advised of the actions they should take if they become unwell ('sick day rules') and advised to contact the GP practice/diabetes team if they have any queries.***

## **Further Information**

### **'Sick day rules' in type 2 diabetes resources for healthcare professionals:**

ABCD SGLT2 inhibitors in people with type 2 diabetes: An educational resource for health professionals (page 10)  
[https://abcd.care/sites/abcd.care/files/site\\_uploads/Resources/Position-Papers/SGLT2-inhibitors-ABCD.pdf](https://abcd.care/sites/abcd.care/files/site_uploads/Resources/Position-Papers/SGLT2-inhibitors-ABCD.pdf)

### **'Sick day rules' in type 2 diabetes resources for patients:**

Diabetes UK website

<https://www.diabetes.org.uk/guide-to-diabetes/life-with-diabetes/illness>

TREND sick day rules – 'Type 2 diabetes - what to do when you are ill' patient information leaflet (updated in response to coronavirus)

<https://trenddiabetes.online/trend-uk-releases-updated-sick-day-rules-leaflets/>

Type 2 diabetes sick day rules produced by the London Diabetes Clinical Network which link specifically to coronavirus

<https://www.england.nhs.uk/london/wp-content/uploads/sites/8/2020/04/3.-Covid-19-Type-2-Sick-Day-Rules-Crib-Sheet-06042020.pdf>

## **Contacts**

For any further queries, the **Community Diabetes Specialist Nurse Team** (based at The Robert Hague Diabetes and Endocrine Centre, BHNFT) can be contacted on the following number: 01226 240086.

## **References**

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2. Association of Clinical Diabetologists – Letter from the National Diabetes Inpatient COVID Response Team highlighting the need to maintain patient safety whilst accelerating patient flow through the system including preventing avoidable admissions and readmissions. Available at: <https://abcd.care/coronavirus>. Accessed <24.05.2022>
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4. MHRA Drug Safety Update 18 March 2020. SGLT2 inhibitors: monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness. Available at: <https://www.gov.uk/drug-safety-update/sglt2-inhibitors-monitor-ketones-in-blood-during-treatment-interruption-for-surgical-procedures-or-acute-serious-medical-illness> Accessed <24.05.2022>
5. MHRA Drug Safety Update December 2021. Dapagliflozin (Forxiga): no longer authorised for treatment of type 1 diabetes mellitus. Available at: <https://www.gov.uk/drug-safety-update/dapagliflozin-forxiga-no-longer-authorised-for-treatment-of-type-1-diabetes-mellitus> Accessed <24.05.2022>
6. Barnsley Joint Formulary. Available at: <http://www.barnsleyformulary.nhs.uk/> Accessed <24.05.2022>
7. Guidelines for approved choice of Blood Glucose Testing Strips, Meters and Lancets. Also includes guidance for self-monitoring of blood sugars and ketones. Available at: [https://best.barnsleyccg.nhs.uk/clinical-support/medicines/prescribing-guidelines/Blood\\_Glucose\\_Test\\_Strips.pdf](https://best.barnsleyccg.nhs.uk/clinical-support/medicines/prescribing-guidelines/Blood_Glucose_Test_Strips.pdf) Accessed <24.05.2022>

### **Development Process**

This guidance was developed by the Barnsley CCG Medicines Management Team on 19<sup>th</sup> May 2020 (updated May 2022) in consultation with the Endocrinologists at BHNFT, community Diabetes Specialist Nurses and Sue Jones, Lead Nurse for Diabetes, Primary Care. The 2022 update was ratified by the Barnsley Area Prescribing Committee on 14<sup>th</sup> September 2022.