

Patient Safety Information Guidance – SGLT-2 inhibitors for Diabetes

Diabetes

What is the aim of this leaflet?

This leaflet contains essential safety information that should be known to all patients who are prescribed SGLT-2 inhibitors. This is to ensure that you are fully aware of all aspects of their use, including the potential side effects.

Please note that this leaflet is not a substitute for the 'patient leaflet' which is included with the medication.

Which drugs are SGLT-2 inhibitors?

Currently available SGLT-2 inhibitors are: Empagliflozin (Jardiance), Canagliflozin (Invokana), Dapagliflozin (Forxiga) and Ertugliflozin (Steglatro). All have received NICE recommendation for adults with type 2 diabetes mellitus.

How does this medication work?

This medication helps control your blood sugar level by making your kidneys eliminate increased amount of sugar (glucose) through your urine.

Since you eliminate higher amounts of sugar in your urine, if you are doing urine tests, they will be 'positive' for glucose (sugar). You should not be worried about this, as this does not necessarily mean that your blood glucose is high.

Does this medication cause low blood glucose level (hypoglycaemia or hypos)?

This medication, in itself, does not cause low blood glucose. It merely helps to stabilize high blood glucose levels.

However, if you are on insulin or tablets like glimepiride or gliclazide, this medication can enhance their effect and thereby increase the risk of hypoglycaemia.

If you are on any of these medications, please ask your doctor or specialist to provide more information about hypoglycaemia including what symptoms to expect and how to treat this immediately, if you need to.

When SGLT-2 inhibitors are being prescribed, please inquire of your doctor or specialist, if there is a need for you to adjust any of your diabetes medications.

The prevention of infection is a major priority in all healthcare and everyone has a part to play.

- **Please decontaminate your hands frequently for 20 seconds using soap and water or alcohol gel if available**
- **If you have symptoms of diarrhoea and/or vomiting, cough or other respiratory symptoms, a temperature or any loss of taste or smell please do not visit the hospital or any other care facility and seek advice from 111**
- **Keep the environment clean and tidy**
- **Let's work together to keep infections out of our hospitals and care homes.**

What other precautions shall I take while I am on this medication?

A. Dehydration

This medication can cause you to urinate more often or pass a higher amount of urine. This can cause dehydration, especially during hot weather and periods of illness.

In view of this, it is important to take adequate amount of non-sugary drinks to keep yourself well hydrated.

However, if you have conditions like heart failure, kidney failure or liver disease, please consult your doctor about specific guidance on how much fluid you should be taking per day.

B. Genital and urinary tract infections

As this medication increases the sugar content of your urine, this may attract germs (bacteria and fungi) and result in urinary tract infections, or more commonly genital tract infections like thrush.

The likelihood of an infection is highest during the period shortly after starting the medication, although it may occur at any time during the treatment.

Most infections are mild and respond well to treatment. Medications such as anti-fungal creams can be obtained over-the-counter to treat genital thrush.

The most common symptoms are itching, redness and tears in the genital skin, making it uncomfortable to sit down, pass urine or have sexual intercourse. Urinary tract infections can cause burning while passing urine.

Severe infection in men can present in the form of an extremely rare condition called 'Fournier's Gangrene'. It is more likely to occur in men with other severe medical conditions, and usually starts as an area of redness or a sore in the genital or groin area and spreads rapidly and makes you feel unwell. You must seek urgent medical attention if you are on this medication and develop such symptoms.

The good news is that it is easy to minimise your chances of infection by following simple hygiene precautions described below:

- Avoiding the use of conventional soaps, shower gels and bubble baths to clean your private areas. These products deprive the genital skin of its moisturising oils, resulting in small cracks, which provide access to germs. It is preferable to wash with soap substitutes which help retain the essential skin moisture
- Avoiding the use of 'wet wipes' as these too can be harsh on the delicate genital skin
- Avoid 'shaving' the genital skin as this can cause injury and small cracks which allow the entry of germs. Trimming the hair is a safer option
- Women should avoid using vaginal douches and feminine hygiene products which can kill 'healthy' bacteria that protect you from infection
- Men should retract the foreskin when washing and dry gently with a towel before replacing

Please consult your doctor or specialist if you have persistent symptoms for over 1 week or recurrent genital infections despite ensuring good hydration and hygiene. This would require further assessment and appropriate decisions regarding withholding your medication temporarily or permanently.

C. If you have problems with 'diabetic foot disease' or reduced circulation in your feet

Highlight this to your doctor while being prescribed this medication. Most studies have shown that these medications do not cause an increase in the risk of severe foot disease or foot amputation, but the risk differs from patient to patient and your doctor may assess your individual risk in detail before prescribing this medication.

Ensure that you follow general foot care advice diligently. You can consult your doctor or podiatrist for more details if you seek education on preventive foot care.

D. Risk of diabetic ketoacidosis (DKA)

DKA is a serious complication of diabetes, involving high blood sugar and a buildup of ketones and acids in your blood. The most common symptoms are nausea, vomiting, abdominal pains, fast breathing, drowsiness or fever. It is usually triggered by an acute infection, vomiting, fasting due to illness or before a surgical procedure.

If you are on this medication and develop any of the above symptoms, please seek urgent medical attention.

In patients on SGLT-2 inhibitors, DKA can occur even with normal blood glucose concentrations. However, it is a very rare complication of SGLT-2 inhibitors.

E. Sick-day rules

The risk of DKA while being on SGLT-2 inhibitor therapy can be further minimized by understanding when there is a risk (sick day rules) and adopting the following safety practices:

When do the sick-day rules apply?

- Period of acute illness, for example, if you develop an infection, diarrhoea or vomiting
- Poor oral intake due to illness
- Fasting overnight prior to a surgical procedure

What do the sick-day rules comprise of?

During any of the above situations, patients with diabetes are at a higher risk of DKA. Hence, if you are in any of the above situations, you must stop SGLT-2 inhibitors and seek medical advice on when it is safe to restart the tablets.

Are there any other medications that I must stop during illness or surgery?

- Following is the list of medications to which the 'sick-day rules for diabetes' apply, for example, it is recommended that you stop the following medications if you are in any of the situations listed above:
 - i. Diabetes medications, for example, metformin, SGLT-2 inhibitors. Do not stop taking insulin
 - ii. Blood pressure tablets, for example, medicines ending with '-artan' or '-pril'
 - iii. Diuretics (water tablets), for example, furosemide, bumetanide, spironolactone
- If you have blood glucose testing equipment, you should increase the number of times you check your blood glucose level. If they run too high or low, please seek medical advice
- If you have discontinued any of the above medications, restart them as soon as you are well and eating normally. Please seek medical advice if you continue to feel unwell after 48 hours

References

1. Rosenstock J, Ferrannini E. Euglycemic Diabetic Ketoacidosis: A Predictable, Detectable, and Preventable Safety Concern With SGLT2 Inhibitors. *Diabetes Care*. 2015 Sep;38(9):1638-42. doi: 10.2337/dc15-1380. PMID: 26294774.
2. MHRA (2016) SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis. Medicines and Healthcare products Regulatory Agency. Available from <https://www.gov.uk/drug-safety-update/sglt2-inhibitors-updated-advice-on-the-risk-of-diabetic-ketoacidosis>
3. MHRA (2017) SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation (mainly toes). Medicines and Healthcare products Regulatory Agency. Available from <https://www.gov.uk/drug-safety-update/sglt2-inhibitors-updated-advice-on-increased-risk-of-lower-limb-amputation-mainly-toes>
4. MHRA (2019) SGLT2 inhibitors: reports of Fournier's gangrene (necrotising fasciitis of the genitalia or perineum). Medicines and Healthcare products Regulatory Agency. Available from <https://www.gov.uk/drug-safety-update/sglt2-inhibitors-reports-of-fournier-s-gangrene-necrotising-fasciitis-of-the-genitalia-or-perineum>