

This leaflet has been developed to explain to people starting SGLT-2 inhibitors what they are, the possible side effects and when to seek help (September 2020)

What are SGLT-2 inhibitors?

- Sodium glucose cotransporter inhibitors (SGLT-2 inhibitors) are sometimes known as 'gliflozins'.
- They reduce blood glucose levels by acting on the kidneys to increase the amount of glucose excreted in urine.
- In addition reductions in blood pressure and weight can occur.
- More recently they have been found to reduce the development and progression of kidney disease and heart failure, even in those without diabetes.
- In the UK the available gliflozins are marketed under the following names:

Canagliflozin (Invokana) 100-300mg Dapagliflozin (Forxiga) 5-10mg
Empagliflozin (Jardiance) 10-25mg Ertugliflozin (Steglatro) 5-15mg

What to do when you start SGLT-2 drugs

- Discuss benefits and cautions with a health professional (nurse, doctor or pharmacist)
- This understanding should include information on the type of diabetes you have, how SGLT inhibitors work, why some people can get diabetic ketoacidosis, signs and symptoms of early DKA, sick day guidance, when to start, stop and when to restart SGLT-2 drugs and how to get blood ketone checks when needed in your area.
- You should have contact details of a health professional who can give you some advice when you are not well and want some help.
- Other diabetes medications like sulphonylurea and insulin may have to be reduced to avoid sugars going too low.
- If you take water tablets (diuretics) or medication for high blood pressure, these should be reviewed periodically, especially if dehydration is a concern.

How can you recognise, confirm or manage DKA?

You need to consider that you might have DKA if you have the following:

- Vomiting
- Abdominal pain
- Unexpected drowsiness or extreme tiredness
- Over breathing and possible smell or taste of pear drops (acetone) on breath
- N.B. DKA is possible even if glucose levels are near normal. Do not rely on urine ketone checks, but have blood ketones measured at surgery or local hospital.

If DKA is confirmed, the you may require hospitalisation and treatment with intravenous fluids and insulin.

Some tips that will help you when you are unwell

When you are **unwell and unable** to eat and drink as normal :

- Have your blood ketones measured at the surgery or local hospital unless you had direct access to a blood ketone meter.
- If blood ketones are higher than 0.6 mmol/L, contact your doctor or go to A and E.
- Take half glass of milk, fruit juice, yogurt or calorie rich soup (250 to 500 ml every 4-6 hours) if you are not able to eat and cover the intake with half the normal dose of insulin if you are taking insulin.
- Drink plenty to avoid dehydration until you are able to obtain medical attention.
- Seek medical advice if you have any ongoing infection or illness.
- In addition to gliflozins, you may need to temporarily withhold other medications.

Urine infections (UTIs)

- The risk of UTIs can be reduced by increasing your fluid intake (unless told not to by your health professional), fully emptying your bladder by repeat urination. Some people find sugar free cranberry juice of help.
- Symptoms of UTIs include
 - Fever or chills
 - Increased frequency of passing urine or burning sensation when passing urine
 - Pain in loins or blood in urine
- If you have concern, seek medical advice

Side-effects of SGLT-2 medicines

- For most people the benefits of taking this medication outweigh the possible side effects and include reduction in the risk of heart attack, heart failure and kidney failure. However, it is important, as with all medications, to be aware of possible side effects and what to do about them.
- Main side effect:
 - These drugs can cause genital infections (thrush) and less commonly urine infections in some cases. These are more common in women than men and thrush can be treated with over-the-counter medications from pharmacies.
- There are a couple of more uncommon adverse events noted in people with diabetes:
 - Diabetic Ketoacidosis (DKA): This is a serious condition in which acidic substances called ketones build up in the body to dangerous level. It is a serious complication of type 1 diabetes but can occur less commonly in type 2 diabetes also.
 - In some studies they have been reported to be associated with foot problems and therefore may need to be avoided in people with active diabetic foot problems (infected ulcer, or active problem with foot circulation)

What can trigger a DKA in someone on SGLT-2 inhibitors?

- Acute illness & infections
- Starvation or fasting (including if actively trying to lose weight or on ketogenic or low carb diet)
- Excessive exercise
- Alcohol excess or recreational drug use
- Surgery (including pre-op fasting)
- Omitted, forgotten or reduced insulin
- Diarrhoea and vomiting causing dehydration

When to stop/restart treatment with SGLT inhibitors

- Most people cope well with the medication but there may be some instances when it may need to be temporarily or even permanently stopped. If you develop any of the following please contact our healthcare professional for advice:
 - Acute medical admission
 - Admission for elective surgery/procedure requiring starvation
 - Vomiting
 - Dehydration
 - Development of acute diabetes foot issues
- Restart the treatment as advised - usually after 1-2 weeks.
- Do not restart if you develop DKA on SGLT-2 inhibitors.

Genital Infections e.g. thrush

- There is a greater risk of genital infections with gliflozins, more common in women than men. Symptoms include; vaginal soreness, rash-redness on penis or foreskin.
- The following actions can reduce your risk:
 - Avoid washing area with warm water
 - Avoid perfumed soaps, shower gels or douches
 - Avoid latex condoms, spermicidal creams or lubricants which can cause irritation
 - Avoid tight fitting underwear
 - Favour cotton loose fitting underwear
 - Wash hands thoroughly after using toilet
- If you are concerned you may be suffering with a genital infection – antifungal treatment (cream/pessary) is available from your local pharmacy. Your sexual partner will also require treatment if he or she has symptoms. Intercourse should be avoided till both partners are clear of infection. Once treated these infections don't tend to recur if glucose control improves.
- Very rarely people have developed a more serious bacterial infection that requires urgent treatment. has been seen. If you have severe pain, worsening redness, widespread swelling in groin or genital areas, seek help.

Development of foot complications

- There is a possible increase in foot complications in patients at high risk, and therefore good foot care is recommended.
- If you have an active foot problem e.g. infected ulcer, circulatory problem causing rest pain or skin discoloration, withhold the SGLT-2 drugs until advised by a doctor or member of the diabetic foot team.

SGLT-2 inhibitors should be avoided if:

- You are pregnant or breast feeding
- At risk of becoming pregnant whilst using the drugs e.g. sexually active but not using any contraception.