

Top Tips and Recommendations for use of Sodium Glucose

Co-transporter 2 inhibitors (SGLT2i) in people with Type 2 Diabetes (T2DM) For Glycaemic Control

INTRODUCTION

In several drug trials various members of the SGLT2i class have been shown to have cardio renal protective effects over and above their glycaemic effectiveness. Data on these cardio renal effects is emerging rapidly and this may be reflected in changes to the licensing arrangements for individual members of this class.

This document is only designed to be used for the prescription of SGLT2 inhibitors within each individual drug's current licence for glycaemic control in T2DM.

The prime purpose of this guide is to ensure that, where an SGLT-2i is prescribed in a person with type 2 diabetes for management of glycaemic control, it is undertaken safely. This can be achieved by ensuring that these agents are only prescribed for the appropriate patients and that the appropriate information is given to patients to ensure safety.

It is important to note this is only a guide and not exhaustive, appropriate clinical judgement and referral to other reference sources may be appropriate in individual patient cases.

What are SGLT2 inhibitors?

SGLT2 inhibitors (SGLT2i) are an established class of medications for the treatment of diabetes which act by preventing the absorption of glucose and sodium, mainly from the proximal renal tubule in the kidney. Glucose and sodium are, therefore, lost in urine.

People do not become hyponatraemic (unless on diuretics as well) as most of the sodium is reabsorbed in the distal tubule.

This effect results in decreasing the blood glucose level, weight loss, an osmotic diuresis and a drop in blood pressure. These drugs have been licensed and used widely in people with T2DM and have shown significant cardiovascular and renal benefits in different subsets of this group of patients.

When initiating SGLT2 inhibitors: information for the patient

Treatment with SGLT2 inhibitors should be initiated only after ensuring adequate understanding of the person in the following aspects:

- Discuss individualised benefits of taking SGLT2 inhibitors
- Side effects and sick day rules
- Foot care
- Drink plenty of fluids to avoid dehydration unless you have been told to restrict fluids by your healthcare professionals due to heart or kidney problems or some other reason

When initiating SGLT2 inhibitors: Prescribing considerations

Glucose lowering medications that may cause hypoglycaemia, such as insulin and sulphonylureas, should be reviewed and consideration should be given to reduce the dose when an SGLT2 inhibitor is started, particularly if the individual's HbA1c is at target when the treatment is being initiated. If the insulin requirement reduces considerably, one should be cautious of a higher risk of developing DKA. The healthcare professional should review diuretic and anti-hypertensive therapy periodically if hypertension improves or if there is postural hypotension.

Who is likely to benefit most from SGLT2 inhibitor treatment?

It is important to select the right patient for SGLT2 inhibitor therapy and avoid in others who may be at high risk of DKA.

The following patients are likely to benefit most:

- Adults above 18 years with T2DM and one or more of the following:
 - established / high risk of cardiovascular disease
 - chronic kidney disease with albuminuria
 - history of heart failure
 - inadequate glycaemic control with need to minimise hypoglycaemia
 - inadequate glycaemic control with need to minimise weight gain / encourage weight loss
- Patients with a clear understanding of the risks associated with SGLT2 inhibitors and how to reduce those risks and follow sick day rules

Who is likely to be at risk with SGLT2 inhibitors?

Use with CAUTION in the following situations:

- Past history of active foot disease/foot ulceration
- Existing diabetic foot ulcers
- Previous lower limb amputation
- People at risk of hypotension/hypovolaemia (e.g. elderly)
- Person adhering to a ketogenic/low calorie/low carbohydrate diet
- History of PAD
- Body mass index under 25 kg/m² (under 23 kg/m² in South Asian patients)
- Person considered at high risk of acute effects of hyperglycaemia (such as dehydration due to non-adherence to medication)
- Person with very high level of HbA1c >86 mmol/mol
- People diagnosed with or at risk of frailty
- Cognitive impairment or use of a medication compliance aid as this may interfere with the adequate understanding required to follow sick day rules and take action to prevent and identify DKA
- On long term or recurrent courses of steroids
- Long duration of diabetes (generally over 10 years from diagnosis)
- Raised haematocrit
- Potential for pregnancy
- Recent weight loss
- Severe hepatic impairment
- Recurrent UTIs

AVOID in the following situations:

- Acutely unwell
- Past history of diabetic ketoacidosis
- Active foot disease
- Eating disorder
- eGFR lower than allowed in the up-to-date licensing of the medication being considered
- Person with excess alcohol consumption or IVDU
- Unwell person (acute medical illness including COVID-19, surgery or planned medical procedure)
- Any diagnosis or suspicion of diabetes due to other causes, including T1DM, latent autoimmune diabetes (LADA), other genetic causes of diabetes, known pancreatic disease or injury, or people who rapidly progressed to needing insulin within 1 year of diagnosis
- Pregnant, breast feeding, female in the child-bearing years and sexually active without contraception
- Age <18 years
- Suspected or possible T1DM except under specialist supervision (dapagliflozin 5 mg only)
- Inpatient with acute vascular event who is not stable



Produced by Claire Davies, September 2021

Updated October 2021. For review March 2023

For any queries/feedback contact:

claire.davies62@nhs.net

NHS
Northern England
Clinical Networks

| SGLT2 Inhibitor | Dose (When using in T2DM) | Dose Adjustments (When using in T2DM) | | | | |
|--|---|--|--|--|--|---|
| | | eGFR > 60 | eGFR 45-59 | eGFR 30-44 | eGFR <30 | |
| | | | | Note glycaemic benefit will be limited for all SGLT2i below eGFR of 45ml/min as the glucose lowering efficacy of SGLT2i therapy is dependent on renal function. Further glycaemic control may be required. | Hepatic Impairment | |
| Canagliflozin PIL/SPC | 100mg once daily Increased if tolerated to 300mg once daily if required Preferably before breakfast | Initiate 100mg, titrate to 300mg if needed | Initiate/continue with 100mg once daily only | Not recommended for glycaemic control in T2DM. Initiate/continue with 100mg once daily. Further glycaemic control may be required. | Not recommended for glycaemic control in T2DM. Continue established treatment with 100mg but do not initiate. Can continue until dialysis or transplant if ACR >30mg/mmol when eGFR falls below 30. Stop if dialysis/transplant. Further glycaemic control may be required. | No dose adjustment necessary if mild/moderate impairment. |
| Empagliflozin PIL/SPC | 10mg once daily Increased up to 25mg once daily if necessary. With or without food <i>Initiation is not recommended in adults >85 years</i> | Initiate 10mg, titrate to 25mg if required | Do not initiate. For those already taking empagliflozin, continue with 10mg only. | Not recommended for glycaemic control in T2DM. Can continue with 10mg OD if person also has decompensated HF/REF down to eGFR of 20ml/min. Do not initiate if eGFR <20ml/min. Further glycaemic control may be required. NB: NICE TA for Empagliflozin in HF awaited – expected February 2022. | Therapeutic experience in severe hepatic impairment is limited and therefore use is not recommended by manufacturer. | |
| Ertugliflozin PIL/SPC | 5mg once daily Increased to 15mg once daily if necessary and if tolerated Dose to be taken in the morning | Initiate 5mg, titrate to 15mg if needed | Do not initiate. For those already taking ertugliflozin continue with 5mg or 15mg. | Not recommended | Not recommended | |
| Dapagliflozin PIL/SPC | 10mg once daily With or without food | Initiate 10mg | | Not recommended for glycaemic control in T2DM. Can continue with 10mg OD if person also has decompensated HF/REF or CKD down to eGFR of 15ml/min. <i>However, it is worth noting that in the DAPA-HF trial no patients with an eGFR <30ml/min were included.</i> Do not initiate if eGFR <15ml/min. Further glycaemic control may be required. | Initial dose 5mg daily in severe hepatic impairment, can increase to 10mg according to response/tolerability | |

Reducing risk – patient education, sick day rules

When a person with diabetes is not well and is unable to eat and drink as normal, some simple rules can prevent further deterioration or DKA.

- If ill with diarrhoea, vomiting, fever or unusual drowsiness, STOP SGLT2 inhibitors and don't restart until feeling better and eating/drinking fluids normally
 - Restart only AFTER patient has been eating normally for AT LEAST 24 HOURS AND no longer acutely unwell
- Drink plenty of water/sugar-free fluid to avoid dehydration.
- Seek medical advice if particularly unwell with infection or illness
- Stop SGLT2 inhibitors prior to surgery—as advised by pre-op team

Pregnancy and Breast-feeding

AVOID – toxicity in animal studies

Monitoring Requirements

- Renal function – before treatment and at least annually thereafter and before initiation of drugs that may reduced renal function and periodically thereafter
- Volume status and electrolytes

Class Side Effects:

Common:

- Increased risk of UTI
- Polydipsia
- Polyuria
- Urinary disorders
- Volume depletion effects (thirst, postural dizziness, hypotension, dehydration)

Uncommon but **serious**:

- Lower limb amputation
- DKA
- Fournier's Gangrene

Please see individual drug monograph in BNF/SPC for a complete side-effect profile – see hyperlinks in table above.

SGLT2i Use in HF and CKD

Recent clinical trials have shown promising results for use of SGLT2i in HF and CKD in people with and without diabetes. It is to be expected you will see these agents prescribed for these indications. It is key to check what indication the drug is being used for and document this to ensure monitoring and follow up is appropriate. These indications are currently outside the scope of this document and require specialist input. For further advice relating to SGLT2i use for these indications contact the relevant specialist teams.

Additional Important safety information – Please see hyperlinks for more detailed advice:

- [MHRA/CHM advice \(updated April 2016\): SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis \(DKA\)](#)
 - People should be informed on the signs and symptoms of DKA, discontinue treatment with the SGLT2 inhibitor immediately if DKA is suspected or diagnosed
- [MHRA/CHM advice \(MHRA/CHM advice March 2017\): SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation \(mainly toes\)](#)
 - SGLT2i's may increase the risk of lower-limb amputation (mainly toes). All people taking an SGLT2i should be counselled on good preventive foot care. Review if lower limb complications develop (e.g. skin ulcer, osteomyelitis, or gangrene). Monitor people with risk factors for amputation, signs and symptoms of water or salt loss.
- [MHRA/CHM advice: SGLT2 inhibitors: reports of Fournier's gangrene \(necrotising fasciitis of the genitalia or perineum\) \(February 2019\)](#)
 - If Fournier's gangrene is suspected, stop the SGLT2 inhibitor and urgently start treatment (including antibiotics and surgical debridement as required)
- [MHRA/CHM advice: SGLT2 inhibitors: monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness \(March 2020\)](#)
 - SGLT2 inhibitor treatment should be interrupted in people 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 person's condition has stabilised

