

West Yorkshire Guideline for the Safe and Appropriate Use of Sodium Glucose Co-Transporter 2 inhibitors (SGLT2-i) for Adults

What are SGLT2 inhibitors?

SGLT2 inhibitors are an established class of medications for the treatment of type 2 diabetes, heart failure and chronic kidney disease 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.

What are the benefits of SGLT2 inhibitors?

Clinical trials using SGLT2 inhibitors have provided strong evidence in the trial populations for reduced risk of major cardiovascular, renal and heart failure events.

There are many benefits to these agents to people living with diabetes:

- weight loss, up to 3kg of body weight can be seen.
- blood pressure reductions of 3-5mmHg seen in the systolic blood pressure.
- Improvements in blood glucose with reductions in HbA1c of up to 10mmol/mol (1.0%) in people with good renal function*

*there is limited efficacy in people with an eGFR<45ml/min/1.73m².

If the person is not on medications that puts them at risk of hypoglycaemia already (insulin, sulphonylureas or meglitinides) there is minimal risk of hypoglycaemia.

Which SGLT2 inhibitors do I use?

SGLT2 inhibitors have licences for treatment of insufficiently treated type 2 diabetes, chronic kidney disease (CKD) (with and without type 2 diabetes) and symptomatic chronic heart failure (HF) irrespective of ejection fraction (with or without type 2 diabetes). SGLT2 inhibitors have also been shown to reduce the risk of cardiovascular events in people living with type 2 diabetes and atherosclerotic cardiovascular disease (ASCVD) i.e., previous MI, previous stroke, and peripheral arterial disease. **Note: traffic light classification differs depending on the indication.**

Two or Three significant co-morbidities (Diabetes, HF (irrespective of EF) and/or CKD)

1st line: Dapagliflozin

2nd line: Empagliflozin

(canagliflozin and ertugliflozin have fewer licensed indications and their use is mainly limited to glucose control in type 2 diabetes)

NICE criteria for use in Chronic Kidney Disease (CKD)

	With Type 2 Diabetes	Without type 2 Diabetes
dapagliflozin 10mg once daily or empagliflozin 10mg once daily	eGFR 20-90ml/min/1.73m ² recognising that glycaemic benefits will be limited at an eGFR <45ml/min/1.73m ²	eGFR 20-44 ml/min/1.723m ² or eGFR 45-90ml/min/1.73m ² and UACR ≥ 22.6mg/mmol

Licences for the SGLT2 inhibitors medications are changing rapidly. Always prescribe in line with product license, including drug combinations when used for diabetes. The information was correct at the time of publication.

Looking to Start an SGLT2 inhibitor

Discuss individualised benefits of taking an SGLT2 inhibitor and document the indication at initiation.

Check that this is the right drug for the person

Caution in all in the following situations:

- People living with or at risk of frailty –these drugs can be efficacious for those at high cardiovascular or renal risk, particularly those with heart failure, they also have a low hypoglycaemia risk when used alone or with agents that don't cause hypoglycaemia. You should however think about implications of weight loss and risks of candidiasis, increased urinary incontinence, increased risks of euglycemic diabetic ketoacidosis and risks with fluid depletion.
- If history of: kidney transplant, polycystic kidney disease; on immunological/immunosuppressant therapy for renal disease; haemodialysis -seek advice from nephrology prior to starting
- Those on loop diuretics (risk of hypotension and dehydration esp. in older people)
- Severe hepatic impairment – check SPC for each drug

In addition to the above caution in people living with diabetes in the following situations:

- Person adhering to a ketogenic diet, recent weight loss or people intermittently fasting (more important if older person or has CKD or on diuretics) e.g., during Ramadan, should consider withholding medication or introducing ketone testing.
- People on steroid therapy (either IV or oral)
- Body mass index under 25kg/m² (under 23kg.m² in south Asian people)
- Person considered at high risk of acute effects of hyperglycaemia (e.g., dehydration may be caused due to non-adherence to other medications which will be an additive risk for those on SGLT2 inhibitor therapy)
- Person with very high HbA1c >86mmol/mol (~10% in old HbA1c)
- Cognitive impairment: Ensure adequate understanding to take action to prevent and identify DKA

Avoid in all in the following situations:

- eGFR lower than allowed in the up-to-date licensing of the medication being considered
- Person with excess alcohol consumption or intravenous drug use
- Unwell person, inpatient or otherwise (e.g. acute medical illness including sepsis, COVID-19, acute vascular event and still unstable, dehydration, surgery or planned medical procedure)
- Pregnancy or breast feeding (females of child-bearing potential should be counselled on risks in pregnancy and to withhold the medication if they are planning pregnancy)
- Eating disorder - unless specialist diabetes team are happy for the person to be initiated on or to continue therapy (seek specialist advice)
- Age <18 years
- Active foot disease (infection, ulceration, or ischaemia) unless the specialist team have advised to continue or have reinitiated.

In addition to the above avoid in people living with diabetes in the following situations:

- History of diabetic ketoacidosis (DKA) or euglycaemic DKA - unless a clear cause was identified, and the specialist teams involved believe that benefit outweighs risk of continued care. Refer to SPC.
- Type 1 diabetes unless specifically indicated by specialist team (off licence use)
- Any diagnosis or suspicion of diabetes due to other causes, including T1D, a 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.

If a person is suitable to start the SGLT2 inhibitor then discuss with them the risks and benefits of the medications so that they are able to make an informed decision about their care.

Document your discussions, particularly around informing people of the risks and then document the persons decision about their treatment :

Discuss the most common side effects:

Genital mycotic infections: advise people this is common (≥1/100 to < 1/10) in both sexes. Provide genital hygiene advice and advice on how to self-treat. Most initial cases can be treated with topical antifungals and won't recur. The SGLT2 inhibitor can be continued during treatment. Consider reviewing therapy or prophylactic antifungal therapy if recurrent infections.

Increased urination: advise people to expect Increased frequency and/or increased volume of urine

Volume depletion side effects discuss with people the signs (thirst, postural dizziness, hypotension and dehydration) and advise people that you will take particular care in someone who is older and/or living with frailty. Discuss measuring blood pressure in lying and standing positions in those at risk of falls and those on diuretics

Discuss rare side effects:

Diabetic ketoacidosis (can be euglycemic): advise people that this is a rare (≥ 1/10,000 to < 1/1,000) side effect in people living with diabetes but that it can be serious if it does occur: Inform and advise people living with diabetes about how to prevent, recognise and how to get treatment for diabetic ketoacidosis (see BOX 1)

Lower Limb Amputation: unknown if class effect, increased rates in CANVAS trials for canagliflozin (incidence rate per 100 patient years: 0.34 (placebo), 0.63 (canagliflozin)). In people living with diabetes, encourage routine preventative foot care and ask all people taking SGLT2 inhibitors to report any wounds, discolouration, or tender/painful feet. If they discover any foot problems, they should seek medical attention immediately and therapy should be withheld if significant foot problems arise (such as infection or skin ulcers or ischaemia). High risk people should receive standard education on relevant diabetes foot care.

Fournier's Gangrene: advise people this is a **very rare** (<1/10,000) side effect. In the DECLARE study of 17,160 people for 2 years, reported 1 case in the treatment group and 5 in the placebo group. People should remain alert to any perianal discomfort (pain or swelling) that is moderate to severe and may be accompanied by general malaise. Advise on good genital hygiene and how to seek help if they do develop symptoms.

Fracture Risk: advise people this is rare however in some cases it may be important to monitor bone parameters e.g., in people with CKD calcium, phosphate and PTH would be monitored. Advise people that evidence for this comes only from trial data involving canagliflozin.

Discuss with people the importance of remaining well hydrated unless they are advised to restrict fluids.

Discuss Sick Day rules (see Box 2) and other times when SGLT2 inhibitors may need to be stopped (see Box 3)

Before you prescribe, a few checks. In people living with diabetes review medications that may cause hypoglycaemia, such as insulin, meglitinides and sulphonylureas. If someone is below or at their individualised blood glucose or HbA1c targets, or there is other cause for concern (e.g., high in day variability of blood glucose) consideration should be given to reduce doses when the SGLT2 inhibitor is started (a 50% reduction in dose of meglitinide or sulphonylurea or a 20% dose reduction in insulin may be appropriate). If the insulin requirement reduces considerably, one should be cautious of a higher risk of DKA. Seek A&G from a diabetes specialist if any concerns. The healthcare professional should recheck blood pressure and review diuretic and anti-hypertensive therapy periodically if hypertension improves or if there is postural hypotension. Before initiating, review licences for renal function (NB no additional renal function monitoring should be required for SGLT2 inhibitors above standard monitoring dictated by care plan). The doses below are based on BNF 25/6/25 and manufacturer's licensed doses in electronic medicines compendium dated May '25.

	eGFR ≥60 ml/min/1.73m ²	eGFR 45 to <60 ml/min/1.73m ²	eGFR 30 to < 45 ml/min/1.73m ²	eGFR 15 to <30 ml/min/1.73m ²	eGFR<15 ml/min/1.73m ²
Canagliflozin					
Insufficiently controlled type 2 diabetes mellitus	Initiate with 100mg od and titrate to 300mg od if needed for glycaemic control	Initiate with 100mg od. If already on canagliflozin, reduce dose to 100mg or continue with 100mg.	Initiate with 100mg od. If already on canagliflozin, reduce dose to 100mg or continue with 100mg. Note a reduced glycaemic effect is very likely at this eGFR.	Not recommended in the absence of DKD due to lack of glycaemic efficacy	Not recommended in the absence of DKD due to lack of glycaemic efficacy
Treatment of diabetic kidney disease (DKD) in adults with type 2 diabetes (UKKA have advised to have uACR ≥25mg/mmol and/or eGFR 20-60 ml/min/1.73m ² for use in people living with diabetes)	Initiate with 100mg od and titrate to 300mg od if needed for glycaemic control	Initiate with 100mg od. Continue or reduce to 100mg for people already taking canagliflozin	Initiate with 100mg od. Continue or reduce to 100mg for people already taking canagliflozin	Do not initiate but continue 100mg for patients already taking canagliflozin only in those with a urinary ACR > 30mg/mmol	Do not initiate and continue 100mg for patients already taking canagliflozin only in those with a urinary ACR > 30mg/mmol. can continue until dialysis or renal transplantation.
Dapagliflozin					
Adults for the treatment of insufficiently controlled type 2 diabetes mellitus	Initiate with 10mg od	Initiate with 10mg od	Initiate with 10mg od. Note a reduced glycaemic effect is very likely at this eGFR.	No glycaemic effect is expected at this eGFR. Do not initiate for this indication and discontinue if only for this indication. See renal and heart failure indications.	No glycaemic effect is expected at this eGFR. Do not initiate for this indication and discontinue if only for this indication. See renal and heart failure indications.
Symptomatic chronic heart failure irrespective of ejection fraction	Initiate with 10mg od	Initiate with 10mg od	Initiate with 10mg od	Initiate with 10mg od	Do not initiate but can continue 10mg od.
Chronic kidney disease* (NICE have advised for use: an eGFR 20- 44ml/min/1.73m ² or eGFR 45 – 90 ml/min/1.73m ² and either type 2 diabetes or a UACR ≥22.6 mg/mmol)	Initiate with 10mg od	Initiate with 10mg od	Initiate with 10mg od	Initiate with 10mg	Do not initiate but can continue 10mg od
Empagliflozin					
Insufficiently controlled type 2 diabetes mellitus	Initiate at 10mg od and titrate to 25mg od if needed	Initiate at 10mg. Continue on 10mg or reduce dose to 10mg od in those already taking empagliflozin	Initiate 10mg od. Note a reduced glycaemic effect is very likely at this eGFR.	No glycaemic effect is expected at this eGFR. Do not initiate for this indication and discontinue if only for this indication. See renal and heart failure indications.	No glycaemic effect is expected at this eGFR. Do not initiate for this indication and discontinue if only for this indication. See renal and heart failure indications.
Symptomatic chronic heart failure irrespective of ejection fraction	Initiate at 10mg od	Initiate at 10mg od	Initiate at 10mg od	Initiate 10mg od if eGFR ≥ 20ml/min/1.73m ² . Can continue 10mg od if already taking.	Do not initiate but can continue 10mg od.
Chronic Kidney Disease (NICE have advised for use: an eGFR 20- 44ml/min /1.73m ² or eGFR 45-90ml/min/1.73m ² and either type 2 diabetes or a UACR ≥22.6 mg/mmol)	Initiate at 10mg od	Initiate at 10mg od	Initiate at 10mg od	Initiate 10mg od if eGFR ≥ 20ml/min/1.73m ² . Can continue 10mg od if already taking.	Do not initiate but can continue 10mg od.
Ertugliflozin					
Insufficiently controlled type 2 diabetes mellitus	Initiate at 5mg od and titrate to 15mg if needed for glycaemic control	Initiate at 5mg od and titrate to 15mg if needed for glycaemic control	Do not initiate. Discontinue if already taking	Do not initiate. Discontinue if already taking	Do not initiate. Discontinue if already taking

BOX 1: Diabetic Ketoacidosis (DKA)

Explain that DKA is an uncommon and serious side effect caused by the build-up of ketones which are being produced due to insulin deficiency (absolute or relative). Inform people of the common causes as part of a preventative strategy:

1. Acute Illness/infections
2. Starvation/fasting
3. Carbohydrate deficient diet i.e., ketogenic diets (50-130g of carbohydrate per day)
4. Excessive exercise
5. Alcohol
6. Surgery
7. Illicit drugs
8. Reduced insulin dose (if on insulin)
9. Dehydration

With SGLT2 inhibitors DKA may occur with normal glucose levels

Be aware and make your patient aware of the signs and symptoms of DKA: Nausea, vomiting, abdomen pain, stupor, fatigue, and difficulty breathing. Ketones need to be tested urgently if DKA is suspected. DO NOT USE urine ketone testing. Test capillary ketones if you have access to a ketone meter and if not refer to the hospital for blood ketone testing. If ketones >1.5mmol/L then further tests may be needed to ascertain if the person has a DKA.

BOX 2: Sick Day Rules

To be used when a person with diabetes is not well and unable to eat and drink as normal

1. If ill with diarrhoea, vomiting or fever stop the SGLT2 inhibitor and do not restart until eating/drinking fluids normally.
2. When people with diabetes who take insulin are not able to eat, it might be possible for them to consume milk, fruit juice, yoghurt or soup in place of meals and adjustments may need to be made to usual medication regimens e.g., insulin.
3. Drink plenty of water/sugar free fluids to avoid dehydration for up to 24 hours. If not resolved > 24 hours seek medical advice
4. Seek medical advice if seriously unwell with infection or illness

BOX 3: When to stop SGLT2 inhibitors

When there is an increased risk of DKA:

- a. Acute medical illness, including for COVID-19 infection.
- b. Admission for elective surgery or procedure requiring starvation.
- c. Vomiting and/or diarrhoea
- d. Dehydration

Restart only AFTER the patient has been eating and drinking normally for 24 hours AND no longer acutely unwell. You may need to commence alternative treatments in the interim.

BOX 4: Practical considerations in older people living with frailty

The risks of SGLT2is may be more pronounced or have more impact in older people living with frailty. However, the benefits should not be overlooked:

1. What matters to the person – health goals, beliefs and values? What do they understand about their condition?
2. What are the benefits/risks of treatment – consider using Number Needed to Treat /Number Needed to Harm /Benefits, Risks, Alternatives or do Nothing (BRAN) as part of a shared decision making conversation. For example, for dapagliflozin in CKD it usually takes 13 months to see a benefit so would not be worthwhile starting in someone with life expectancy less than this. Currently there is a lack of evidence for SGLT2 inhibitors in CKD in older people living with frailty so this should be discussed. NNT/NNHs are from clinical trials in younger people.
3. Discuss possibility of urogenital infections and advise people to expect increased frequency and/or increased volume of urine. Consider existing urological issues.
4. Volume depletion side effects - discuss with people the signs (thirst, postural dizziness, hypotension and dehydration). Discuss measuring blood pressure in lying and standing positions in those at risk of falls and those on diuretics. May require down-titration of diuretics/antihypertensives (prioritise RAAS blockade to continue).
5. Check understanding and retention of information e.g. DKA risk, sick day rules and other medication adjustments.

Useful Resources for people living with diabetes:

TREND leaflets (free to register) <https://trenddiabetes.online/resources/>

- Diabetes and your Kidneys
- How to reduce your risk of genital fungal infection
- Type 2 DKA
- Type 2 Diabetes: what to do when you are ill

[Leeds Information for People on SGLT-2 inhibitors Leaflet \(including sick day rules\)](#)

[Leeds Easy Read SGLT2 inhibitor leaflet](#)

[ABCD SGLT2 information](#)

References:

Dashora U, Gregory R, Winocour P, Dhatariya K, Rowles S, Macklin A, Rayman G, Nagi D, Whitehead K, Beba H, De P, Patel DC; ABCD executive committee and Diabetes UK. Association of British Clinical Diabetologists (ABCD) and Diabetes UK joint position statement and recommendations for non-diabetes specialists on the use of sodium glucose co-transporter 2 inhibitors in people with type 2 diabetes (January 2021). Clin Med (Lond). 2021 May;21(3):204-210. doi: 10.7861/clinmed.2021-0045. PMID: 34001571; PMCID: PMC8140708.