

## Initiating SGLT2 Inhibitors for Adults in Type 2 Diabetes and in Chronic Kidney Disease

Following the update to NICE Guidance [NG28 Type 2 diabetes in adults: management](#) in February 2022, the SGLT2 inhibitors (with proven cardiovascular benefit) should now be offered at diagnosis of diabetes for those who have heart failure or established atherosclerotic cardiovascular disease (CVD). In addition, they should be considered at diagnosis for those who are at high risk of developing CVD (QRisk2 or 3  $\geq 10\%$ ).

At any point in the management of diabetes, where there is a change to cardiovascular risk or status change, SGLT2 inhibitors ought to be considered.

### Chronic Kidney Disease (CKD):

Licensed SGLT2s should also be used in the management of CKD where ACE/ARB is optimised to the maximum tolerated dose (unless contraindicated) and:

#### **For Dapagliflozin:**

- people have an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m<sup>2</sup> to 75 ml/min/1.73 m<sup>2</sup> at the start of treatment and:
  - have type 2 diabetes or
  - have a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more.

#### **For Empagliflozin:**

- people have an estimated glomerular filtration rate of:
  - – 20 ml/min/1.73 m<sup>2</sup> to less than 45 ml/min/1.73 m<sup>2</sup> or
  - – 45 ml/min/1.73 m<sup>2</sup> to 90 ml/min/1.73 m<sup>2</sup> and either:
    - ◇ a urine albumin-to-creatinine ratio of 22.6 mg/mmol or more, or
    - ◇ type 2 diabetes.

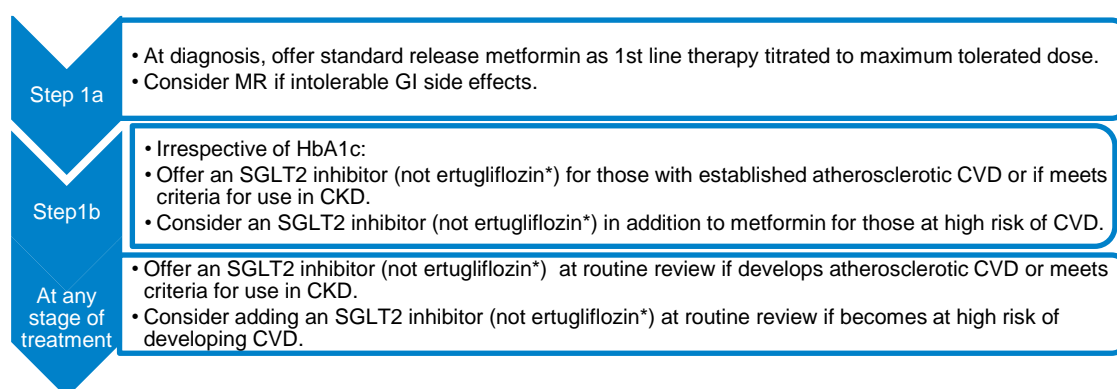
#### **See links for further information:**

Dapagliflozin for treating chronic kidney disease: [NICE TA775](#).

Empagliflozin for treating chronic kidney disease: [NICE TA942](#)

The aim of this guidance is to ensure that SGLT2 inhibitors are added appropriately to established therapy.

**For patients with heart failure, initiation of an SGLT2 inhibitor should be undertaken by or be discussed with Specialist Teams. Please see [Guidelines for the use of Dapagliflozin & Empagliflozin \(SGLT2\) in Heart Failure](#)**



The glucose lowering efficacy of SGLT2 inhibitors is reduced when eGFR is < 45 mL/min/1.73m<sup>2</sup> and is likely absent in patients with severe renal impairment. Therefore, additional glucose lowering treatment should be considered in patients with type 2 diabetes mellitus when eGFR<45.

### Adjusting ORAL medication when adding SGLT2 inhibitor with proven CV benefit for cardiorenal protection

SGLT2 inhibitors with proven cardiovascular benefit indicated for T2 Diabetes:

Dapagliflozin 10mg OD

Empagliflozin 10mg OD, increased to 25mg OD if necessary and tolerated.

Canagliflozin 100mg OD, increased if tolerated to 300mg OD if required.

\*Note that cardiovascular benefits with Ertugliflozin have not been established.

**Please see [BNF](#) and [SmPC](#) for further dose titration and renal impairment adjustment.**

For simplicity, Dapagliflozin 10mg is advocated by our local specialists as no dose titration is required or dose adjustment in renal impairment, and it also has a broad product license. However, you can use an alternative SGLT2 inhibitor such as empagliflozin or canagliflozin if preferred.

Current regime includes:	Suggested adjustment following discussion with patient:	Monitoring needed:	
		HbA1c target met:	HbA1c target not met:
<b>Metformin only</b>	Up titrate to maximum tolerated dose of Metformin and then add SGLT2 inhibitor.	Repeat HbA1c as per normal schedule (6-12months).	Repeat HbA1c after 3 months and escalate treatment if target still not met.
<b>Gliclazide (or other Sulfonylurea)</b>	Add SGLT2 inhibitor and reduce dose of Sulfonylurea by 50% where HbA1c target achieved or if within 10mmol of target. Where HbA1c exceeds target by >10mmol, add SGLT2 inhibitor.	Repeat HbA1c at 3 months.	Repeat HbA1c after 3 months and escalate treatment if target still not met.
		Check fasting blood glucose levels for 1 week after changes. Gliclazide can be reduced or stopped as appropriate.	
<b>Alogliptin/Linagliptin Saxagliptin/Sitagliptin</b>	Swap for SGLT2 inhibitor. if eGFR>45. Add SGLT2 inhibitor. if eGFR <45	Repeat HbA1c as per normal schedule (6-12months).	Repeat HbA1c after 3 months and escalate treatment if target still not met.
<b>Pioglitazone</b>	Add SGLT2 inhibitor.	Repeat HbA1c as per normal schedule (6-12months).	Repeat HbA1c after 3 months and escalate treatment if target still not met.

### Benefits of SGLT2 inhibitors

- Up to 10mmol/mol reduction in HbA1c (dependent on starting level)
- Low incidence of hypoglycaemia (effect proportional to blood glucose)
- Weight loss (up to 3kg)
- Cardioprotective benefit, reduces progression of chronic complications affecting cardiovascular system and kidneys. (N.B. not applicable to ertugliflozin)

SGLT2 inhibitors can drop blood pressure (~5mm/Hg) and so a review of antihypertensives may be necessary.

#### SGLT2 Inhibitors should NOT be used where:

- History of diabetic ketoacidosis (DKA)
- Ketogenic or very low carbohydrate diet
- Currently unwell (acute illness, surgery or planned procedure)
- Pregnancy or risk of pregnancy
- Breast feeding
- Type 1 diabetes

#### SGLT2 Inhibitors should be used with CAUTION where:

- History of persistent or complicated UTI
- Frail and elderly
- Severe hepatic impairment
- Consult [SmPC](#) to see if dose adjustment is required in patients with renal impairment

## Provide information to the patient on:

- Potential side effects and when to seek review notably to report severe pain/tenderness/erythema/swelling in the genital/perineal area and importance of preventative foot care.

Please see [MHRA Drug Safety Updates: SGLT2 inhibitors: reports of Fournier's gangrene](#) and [SGLT2 inhibitors: updated advice on increased risk of lower limb amputation](#)

- Sick day guidance- see below (stop Dapagliflozin if diarrhoea/vomiting or symptoms of DKA and do not restart until eating/drinking normally for at least 24 hours).
- Staying hydrated.

## Risk of DKA and SGLT2 inhibitors

The risk of DKA must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness.

Patients should be assessed for ketoacidosis immediately if these symptoms occur, regardless of blood glucose level.

Test strips for monitoring ketone levels should not routinely be prescribed in T2D patients who take SGLT2 inhibitors. A strong emphasis should be placed on patient education of symptoms of DKA and seeking urgent medical assessment in the event of symptoms rather than encouraging home monitoring.

Please see [MHRA Drug Safety Updates: SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis](#) and [SGLT2 inhibitors: monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness](#)

## Written Information for Patients

Trend leaflet [Type 2 diabetes: What to do when you are ill – Trend Diabetes](#)

Arden's have information leaflets [Medicines and Dehydration "Medicine Sick Day Guidance" and Sodium-glucose Co-transporter (SGLT2) Inhibitors – see appendix for images] that can be personalised and a read code can be input to document that advice has been provided [Y3767 *information given re sick day rules* or Y308a *Medication side-effect education:SGLT2i*].

### Seek advice from Specialist Teams if guidance required.

Specialist Team	Telephone	Email
BaNES DSN	07876 265064	<a href="mailto:ruh-tr.communitydsn@nhs.net">ruh-tr.communitydsn@nhs.net</a>
Swindon DSN	01793 463841	<a href="mailto:SWICCG.CommunityDiabetesService@nhs.net">SWICCG.CommunityDiabetesService@nhs.net</a>
Wiltshire DSN	North, East and West 01248 456 483	<a href="mailto:whc.diabetesnurses@nhs.net">whc.diabetesnurses@nhs.net</a>
	South 012722 425 176	

## References

1. National Institute for Health and Care Excellence. NG203. Chronic kidney disease: assessment and management, updated November 2021. Available from <https://www.nice.org.uk/guidance/conditions-and-diseases/kidney-conditions/chronic-kidney-disease>
2. National Institute for Health and Care Excellence. NG 28. Type 2 diabetes in adults: management, updated March 22. Available from <https://www.nice.org.uk/guidance/ng28>
3. National Institute for Health and Care Excellence. British National Formulary. Accessed May 2022. Available from <https://bnf.nice.org.uk>
4. Summary of Product Characteristics. Accessed May 2022. Available from <https://www.medicines.org.uk>
5. National Institute of Clinical Excellence. TA 775. Dapagliflozin for treating chronic kidney disease. Published March 2022. Available from <https://www.nice.org.uk/guidance/ta775>

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### Medicines and Dehydration "Medicine Sick Day Guidance"

Dehydration is due to a loss of fluid from your body. Vomiting, diarrhoea and fever (high temperature, sweats, shaking) can make you dehydrated. If you are sick once or have diarrhoea once, then you are unlikely to become dehydrated. Having two or more episodes of vomiting or diarrhoea or having a prolonged fever can lead to dehydration.

Taking certain medicines when you are dehydrated can result in you developing a more serious illness.

**Medicines that make dehydration more likely are:**

Diuretics Sometimes called "water pills" eg Furosemide, spironolactone, bendroflumethiazide

**Medicines that can stop your kidneys working if you are dehydrated are:**

ACE inhibitors Medicine names ending in "pril" eg Lisinopril, perindopril, ramipril  
 ARBs Medicine names ending in "sartan" eg Losartan, candesartan, valsartan  
 NSAIDs Anti-inflammatory pain killers eg Ibuprofen, naproxen, diclofenac

**Medicines that make you more likely to have a side effect called lactic acidosis if dehydrated are:**

Metformin A medicine for diabetes  
 SGLT2's Medicine names ending in "gliflozin" eg Canagliflozin, Dapagliflozin, Empagliflozin

**"Medicine Sick Day Guidance"**

If you develop a dehydrating illness, then it is important that you discuss your condition with a medical professional. This may be your GP, Nurse or Pharmacist. You may be advised to discontinue taking medications which lower your blood pressure for a short time and a blood test will be arranged to check your kidney function. Remember to keep drinking small amounts of fluid regularly on your sick days too. If you are only passing small amounts of urine you may need admission to hospital and you should alert your GP to this. Please do not delay calling your GP or the out of hours service if your urine output decreases to only small volumes.

I (<Patient name>) am on the following medications that put me at risk of acute kidney injury if I am dehydrated:  
<Medication>

Please cut out the alert card below and place in your wallet

<p><b>"Medicine Sick Day Guidance" Alert Card</b></p> <p>When you are unwell with any of the following: Vomiting and diarrhoea (unless very minor) Fever, sweats and shaking</p> <p>Contact a medical professional, this may be your GP, Nurse or Pharmacist.</p> <p>If advised, STOP taking the medicines highlighted overleaf.</p> <p>Restart when you are well (usually 24-48 hours of eating and drinking normally)</p>	<p><b>Medicines that need medical advice if you are ill:</b></p> <p><input type="checkbox"/> <b>ACE inhibitors</b> Medicines ending in "pril" eg Lisinopril, perindopril, ramipril</p> <p><input type="checkbox"/> <b>ARBs</b> Medicines ending in "sartan" eg Losartan, candesartan, valsartan</p> <p><input type="checkbox"/> <b>NSAIDs</b> Anti-inflammatory pain killers eg Ibuprofen, naproxen, diclofenac</p> <p><input type="checkbox"/> <b>Diuretics</b> Sometimes called "Water pills" eg Furosemide, spironolactone, bendroflumethiazide, Indapamide</p> <p><input type="checkbox"/> <b>Diabetes</b> Metformin and "gliflozin's"</p>
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Page 1 of 1

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### Sodium-glucose Co-transporter 2 (SGLT2) Inhibitors

Dear <Patient Name>

You are currently taking a SGLT2 inhibitor called <Medication>.

Take this medication according to the instructions from your prescriber. Please make sure you understand how to take the medicine and ask if you have any questions.

This is an effective treatment for diabetes and/or heart failure, but it can have some side effects, including:

- Hypoglycaemia (low blood glucose) – This usually only occurs if taken in combination with other diabetes medicines and your prescriber may therefore need to alter the dose.
- Dehydration – This medicine increases your urine volume so may cause dehydration. To prevent dehydration, you must drink at least two litres of non-sugary drinks a day, unless directed otherwise.
- Genital infections – As this medicine increases the glucose (sugar) in your urine, there is an increased risk of infection, such as genital thrush. Wash your genital area with warm water using non-perfumed soap and avoid wearing tight underwear to reduce the risk of infection.

In rare cases, SGLT2 Inhibitors can cause more serious side effects, including diabetic ketoacidosis (DKA), Fournier's gangrene and lower-limb amputation. Please seek medical advice immediately if you have any of the following:

- Rapid weight loss
- Feeling or being sick, or stomach pain
- Fast and deep breathing
- Sweet or metallic taste in the mouth
- Different odour to your breath, urine or sweat
- Severe pain, tenderness, redness, or swelling 'down below', accompanied by fever or feeling unwell

It is important you attend for regular foot checks whilst taking this medication.

If you become unwell and have vomiting, diarrhoea, or fever, you should stop this medication. You can restart when you are better (eating and drinking normally), however if you remain unwell after 48 hours seek medical advice from your GP, Pharmacist or NHS 111.

The following blood tests are required to monitor your treatment, at least once a year. If you haven't had one in the last year, please book a blood test with your GP practice.

Blood Test	My last result	Reason for test
HbA1c	<Numerics>	To monitor diabetes (if prescribed for diabetes)
eGFR	<Numerics>	To check how your kidneys are working
Creatinine	<Numerics>	To check how your kidneys are working

Notes:

Your next appointment is:

Page 1 of 1