UK Kidney Association

UK Kidney Association Clinical Practice Guideline: Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease

Summary of Recommendations

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Authors:

Working Group co-chairs: Assoc. Prof. William G. Herrington & Dr Andrew H. Frankel

Working Group members: Dr Alexa Wonnacott, Dr David Webb, Mrs Angela Watt, Mr Michael Watson, Mr John Roberts, Assoc. Prof. Natalie Staplin, Dr Alistair Roddick, Dr Alex Riding, Dr Eirini Lioudaki, Dr Apexa Kuverji, Prof. Mohsen El Kossi, Dr Patrick Holmes, Mr Matt Holloway, Prof. Donald Fraser, Dr Chris Carvalho, Prof. James Burton, Prof. Sunil Bhandari

See appendix for list of previous versions/revisions and working group affiliations.

The full guideline is available at:

https://ukkidney.org/health-professionals/guidelines/guidelines-commentaries

Summary of recommendations

RECOMMENDATIONS FOR USE IN PEOPLE WITH AN eGFR ≥25mL/min/1.73m^2		
Section 2	**PEOPLE WITH TYPE 2 DM**	**Grade**
1.	We recommend initiating SGLT-2inhibition* in those with: (a) uACR of ≥25 mg/mmol attributed to diabetic nephropathy (b) Established coronary disease or stable symptomatic heart failure (irrespective of ejection fraction).	**1A**
2.	We recommend initiating SGLT-2 inhibition in those with a uACR of ≥25 mg/mmol attributable to a non-diabetic cause‡	**1B**
3.	We suggest initiating SGLT-2 inhibition to modify cardiovascular risk in those with an eGFR 25-60 mL/min/1.73m^2 and uACR <25 mg/mmol, recognising effects on glycaemic control will be limited.	**2B**
Section 3	**PEOPLE WITHOUT DM**	
1.	We recommend initiating SGLT-2 inhibition* in those with stable symptomatic heart failure (irrespective of ejection fraction).	**1A**
2.	We recommend initiating SGLT-2 inhibition* in those with a uACR of ≥25 mg/mmol, excluding people with polycystic kidney disease or on immunological therapy for renal disease.‡	**1B**
** See section 4 for summary of indications/licensed uses* *‡ DAPA-CKD provides the key clinical evidence and excluded people with a kidney transplant, polycystic kidney disease, lupus nephritis, ANCA-associated vasculitis, and those receiving immunological therapy for renal disease in the last 6 months.*		
RECOMMENDATIONS FOR IMPLEMENTATION		
Sections 2 & 3	**PEOPLE WITH OR WITHOUT DM (excluding TYPE 1)**	**Grade**
1.	We recommend using SGLT-2 inhibitors with demonstrated efficacy for their given indications.*	**1A**
2.	We recommend using clinically appropriate single agent RAS blockade in combination with SGLT-2 inhibition, wherever RAS blockade is indicated and tolerated.	**1A**
3.	We suggest following NICE guidelines on screening for albuminuria (NICE NG203): a single uACR of ≥70 mg/mmol or a confirmed measurement between 25-69 mg/mmol fulfil recommendations for use of SGLT-2 inhibition based on albuminuria.	**2C**
4.	We suggest using uACR to assess for sufficient proteinuria to guide SGLT-2 inhibitor use: reagent strips and protein:creatinine ratio should generally not be used (NICE NG203). We recognise that more pragmatic approaches to identifying risk of kidney disease progression may be necessary whilst local access to uACR measurement is improved.	**2C**
5.	We suggest that when used to slow kidney disease progression or heart failure risk, SGLT-2 inhibition can be continued until the need for dialysis or kidney transplantation arises.	**2B**
6.	We suggest that co-prescription of SGLT-2 inhibition with MRA can be considered, where each are individually indicated.	**2B**

7.	We suggest the beneficial effects of SGLT-2 inhibition on renal outcomes in people with type 2 DM are likely to be a class effect, but there is insufficient data in people without DM to be conclusive.	**2B**
8.	We suggest the beneficial effects of SGLT-2 inhibition on heart failure are likely to be a class effect, irrespective of the presence or absence of DM.	**2B**
Section 5a	**DIABETIC KETOACIDOSIS**	**Grade**
1.	We recommend that people with type 1 DM should only have SGLT-2 inhibitors initiated under the strict direction of the diabetes team.	**1C**
2.	We recommend that people with type 2 DM at greater risk of DKA (defined in Table 5a.1) should have SGLT-2 inhibitors initiated with caution after discussion with the diabetes team.	**1C**
3.	We recommend SGLT-2 inhibitors are discontinued when a patient develops DKA.	**1A**
4.	We suggest that after an episode of DKA and where a clear contributing factor has been identified, there should be discussion with the person and clinical team to establish whether the benefits of re-introducing an SGLT-2 inhibitor outweigh the risks.	**2D**
5.	When initiating SGLT-2 inhibitors, we suggest that individuals should be advised on the signs and symptoms of DKA and be instructed to temporarily withhold SGLT-2 inhibitors and to seek immediate medical advice if symptoms develop.	**1C**
6.	We recommend always offering advice on sick day guidance when initiating SGLT-2 inhibitors and reminding them of this at every medication review.	**1C**
7.	We suggest that individuals taking SGLT-2 inhibitors should be advised against following a ketogenic diet.	**2C**
8.	We suggest that for people who choose to intermittently fast (e.g. for Ramadan), and particularly for those who are elderly, on diuretics or have CKD, consider withholding SGLT-2 inhibitors for the duration of the fasting period and for those people with diabetes ketone testing should be undertaken if unwell.	**2D**
Section 5b	**HYPOGLYCAEMIA**	
1.	We recommend considering reducing the dose of insulin/SUs/meglitinides when initiating SGLT-2 inhibitors to reduce the risk of hypoglycaemia.	**1C**
2.	We recommend that when initiating SGLT-2 inhibitors in people taking SUs (e.g. gliclazide) or meglitinides (e.g. repaglinide) when the HbA1c <58 mmol/mol AND eGFR >45 mL/min/1.73m^2, consider reducing dose of SU or meglitinide by 50% to reduce risk of hypoglycaemia.	**1C**
3.	We recommend that when starting SGLT-2 inhibitors in people taking insulin when the HbA1c <58 mmol/mol AND eGFR >45 mL/min/1.73m^2, consider reducing the insulin dose by 20% to avoid hypoglycaemia.	**1C**
4.	We recommend that when starting SGLT-2 inhibitors in people taking only metformin ± pioglitazone ± DPP-4i/gliptins or GLP-1RA therapy, no dosage adjustment is necessary.	**1C**
Section 5c	**ACUTE KIDNEY INJURY, HYPOVOLAEMIA AND POTASSIUM**	
1.	We recommend that individuals initiated on an SGLT-2 inhibitor do not routinely require an early assessment of renal function or potassium following initiation of treatment.	**1C**

2.	We suggest that if an individual has a renal function assessment within the first few weeks post initiation of an SGLT-2 inhibitor, a decline in eGFR needs to be interpreted with caution and in the context of an expected drug effect to avoid unwarranted discontinuation of treatment.	**2B**
3.	We suggest that individuals on diuretics are counselled on the symptoms of hypovolaemia and advised to seek medical attention if they develop any such symptoms after starting SGLT-2 inhibition.	**2B**
4.	We suggest that clinicians consider an early clinical review and if appropriate a diuretic or antihypertensive dose reduction in individuals they consider at high risk of hypovolaemia.	**2C**
5.	We recommend that SGLT-2 inhibitors are temporarily withheld during acute illness (see sick-day guidance in section 5a.1.2).	**1C**
Section 5d	**PERIPHERAL VASCULAR DISEASE AND AMPUTATION RISK**	
1.	We suggest avoiding initiation of SGLT-2 inhibitors in the presence of active foot disease (infection, ulceration and ischaemia) and withholding treatment in those who develop foot complications whilst taking an SGLT-2 inhibitor.	**2B**
2.	We suggest a shared decision-making approach, with appropriate counselling on risks and benefits of treatment and the importance of routine preventative foot care measures for: • Individuals at high risk of amputation (previous amputations, existing PVD, peripheral neuropathy) • Re-initiation of SGLT-2 inhibitors after treatment and full resolution of a foot complication that occurred whist taking SGLT-2 inhibitors.	**2B**
Section 5e	**FRACTURE RISK**	
1.	In people with CKD treated with SGLT-2 inhibitors, we suggest monitoring of bone parameters including calcium, phosphate and PTH should be performed as appropriate for CKD stage (see NICE NG203).	**2D**
Section 5f	**MULTIMORBIDITY AND FRAILTY**	
1.	We suggest an approach to care that takes account of frailty and multimorbidity where these apply. This can include: • Establishing the person's goals, values and priorities • Consideration of the balance of disease and treatment burden (for example, prognostic benefits in people with limited life expectancy or frailty) • Agreeing an individualised management plan.	**2D**
Section 5g	**MYCOTIC GENITAL INFECTIONS AND FOURNIER'S GANGRENE**	
1.	We recommend that all people are counselled on the risks of mycotic genital infections prior to initiation of SGLT-2 inhibitors.	**1D**
2.	We recommend that all people are counselled on self-care to maintain good genital hygiene.	**1C**
3.	We recommend that all people are counselled on the symptoms of mycotic genital infections and how to seek help including self-management.	**1D**
4.	We suggest that for those individuals with a history of recurrent mycotic genital infections on SGLT-2 inhibition, consideration is given to offering prophylactic anti-fungal treatment, which should be reviewed after 6 months of therapy or earlier if clinically indicated.	**2D**
5.	We suggest that SGLT-2 inhibitor therapy can be continued during the treatment of mycotic genital infections.	**2D**

6.	We highlight the specific MHRA warning and suggest that all people are counselled on the symptoms of Fournier's gangrene and advised to stop SGLT-2 inhibitors and to seek urgent help if they develop such symptoms.	**2D**
Section 5h	**URINARY TRACT INFECTION**	
1.	We recommend temporary discontinuation of SGLT-2 inhibitors when treating pyelonephritis or urosepsis (see sick-day guidance in section 5a.1.2).	**1C**
Section 5i	**CHILDREN, PREGNANCY AND BREASTFEEDING**	
1.	We suggest SGLT-2 inhibitors are not used in children under 18 years of age.	**2D**
2.	We suggest that all women of child-bearing potential are counselled, prior to conception, on the risks of SGLT-2 inhibitors during pregnancy.	**2D**
3.	We suggest SGLT-2 inhibitor therapy is discontinued upon planning, suspicion or confirmation of pregnancy.	**2D**
4.	We suggest SGLT-2 inhibitors are not used in women who are breastfeeding.	**2D**
Section 7a	**PEOPLE WITH TYPE 1 DM**	
1.	We recommend that SGLT-2 inhibitors be initiated in people with type 1 DM, only under the strict direction of the diabetes team.	**1C**
2.	We suggest considering referring people with type 1 DM to the specialist diabetes team, for consideration of an SGLT-2 inhibitor, if they have an eGFR ≥25 mL/min/1.73m^2 and an uACR ≥25 mg/mmol attributable to diabetic nephropathy despite being on maximum tolerated ACEi/ARB.	**2D**
3.	We recommend all people with type 1 DM started on SGLT-2 inhibitors be provided with ketone monitoring, be advised on the signs and symptoms of DKA and to seek immediate medical advice if any of these symptoms develop or ketone levels are >0.6 mmol/L.	**1B**

SUMMARY STATEMENTS		
Section 7b	**KIDNEY TRANSPLANT RECIPIENTS**	**Grade**
1.	There is currently insufficient evidence on safety and efficacy to provide recommendations for use of SGLT-2 inhibition in people with a functioning kidney transplant.	**-**
2.	Any use of SGLT-2 inhibition to treat diabetes mellitus in a kidney transplant recipient should be evaluated by multi-disciplinary discussion.	**2D**
Section 7c	**HEART FAILURE WITH PRESERVE EJECTION FRACTION and ACUTELY DECOMPENSATED HEART FAILURE**	
1.	There is currently insufficient evidence to provide further recommendations for use of SGLT-2 inhibition in people with acutely decompensated heart failure.	**-**

- NICE CKD guidance is available at www.nice.org.uk/guidance/ng203
- For sick day rules also see section 6's template Patient Information Leaflets.

Table abbreviations:

ACEi	Angiotensin-Converting Enzyme Inhibitor
ARB	Angiotensin-II Receptor Blocker
CKD	Chronic Kidney Disease
DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
DPP-4i	Dipeptidyl Peptidase-4 inhibitors
eGFR	Estimated Glomerular Filtration Rate (mL/min/1.73m^2)
GLP-1RA	Glucagon-Like Peptide-1 Receptor Agonist
HbA1c	Glycosylated Haemoglobin
HFpEF	Heart Failure with Preserved Ejection Fraction
LVEF	Left Ventricular Ejection Fraction
MHRA	Medicines and Healthcare products Regulatory Agency
MRA	Mineralocorticoid Receptor Antagonist
NICE	National Institute for Health and Care Excellence
RAS	Renin Angiotensin System
SGLT-2	Sodium-Glucose Co-transporter-2
SU	Sulphonylurea
uACR	Urinary Albumin:Creatinine Ratio

Version number	Date	Details
-	21 Jul 2021	Draft for UKKA Clinical Practice Guideline Committee Review
-	10 Aug 2021	Draft for Public Consultation
-	21 Sept 2021	Draft for Clinical Practice Guideline Committee Review (containing revisions following Public Consultation, updates to NICE CKD guidance and publication of EMPEROR-PRESERVED results and the working group's meta-analysis)
1.0	18 October 2021	First released version