SGLT2i FOR TREATMENT OF CHRONIC KIDNEY DISEASE– GUIDANCE NOTES

TARGET AUDIENCE	Board wide
PATIENT GROUP	Patients with Chronic Kidney Disease

Clinical Guidelines Summary

- Sodium-Glucose co-transporter 2 inhibitors (SGLT2i) have been shown to significantly improve kidney and cardiovascular outcomes in patients with chronic kidney disease (CKD) with and without diabetes
- They have been recommended by the UK Kidney Association, NICE, Kidney Disease Improving Global Outcomes (KDIGO), and the SMC
- They can be safely initiated and continued in patients with CKD with or without diabetes across a broad range of kidney function (indicated by eGFR), and they do not require routine increased monitoring
- Some caution and consideration should be applied in particular patient groups, and patients should be counselled before drug initiation
- Use should not generally be restricted to specialist clinics, but specialist advice can readily be sought if there is uncertainty

These guidance notes are based on the UK Kidney Association Clinical Practice guidelines and incorporate locally relevant SMC advice for prescribing.

UK Kidney Association Clinical Practice Guidelines – SGLT2i in adults with kidney disease (April 2023)

Section 2	PEOPLE WITH TYPE 2 DM	Grade
1.	We recommend initiating SGLT-2 inhibition in people with chronic kidney disease and type 2 diabetes, irrespective of primary kidney disease,* for any of the following 4 clinical scenarios: a) eGFR of 20-45 mL/min/1.73m^2 b) eGFR of >45 mL/min/1.73m^2 and a urinary albumin-to-creatinine ratio (uACR) of ≥25 mg/mmol† c) Symptomatic heart failure, irrespective of ejection fraction d) Established coronary disease	1A
2.	We suggest initiating SGLT-2 inhibition to modify cardiovascular risk and slow rate of kidney function decline in people with an eGFR >45-60 mL/min/1.73m^2 and a uACR of <25 mg/mmol, recognising effects on glycaemic control will be limited.	2B
3.	We suggest clinicians consider initiating SGLT-2 inhibition in people with an eGFR below 20 mL/min/1.73m^2 to slow progression of kidney disease.	2B

Section 3	PEOPLE WITHOUT DM	
1.	We recommend initiating SGLT-2 inhibition in people with chronic kidney disease, irrespective of primary kidney disease,* for any of the following clinical scenarios: (a) eGFR of ≥20 mL/min/1.73m^2 and a urinary albumin-to-creatinine ratio (uACR) of ≥25 mg/mmol† (b) Symptomatic heart failure, irrespective of ejection fraction	1A
2.	We recommend initiating SGLT-2 inhibition to slow rate of kidney function decline in people with an eGFR of 20-45 mL/min/1.73m^2 and a uACR of <25 mg/mmol†.	1B
3.	We suggest clinicians consider initiating SGLT-2 inhibition in people with an eGFR below 20 mL/min/1.73m^2 to slow progression of kidney disease.	2B
** excludes people with polycystic kidney disease, type 1 diabetes, or a kidney transplant* *† urinary protein-to-creatinine ratio of 35 mg/mmol can be considered equivalent*		

SGLT2i and other drugs

- Use a clinically appropriate single agent Renin-Angiotensin System (RAS) blockade in combination with SGLT2i wherever RAS blockade indicated and tolerated
- Co-prescription of SGLT2i with Mineralocorticoid Receptor Antagonist (MRA) can be considered where each are individually tolerated

DKA risk

- SGLT2i use in patients with type 1 DM is contra-indicated
- People with T2DM at greater risk of DKA should only have SGLT2i initiated with caution after discussion with diabetes team
    - HbA1c >86
    - BMI </= 27 kg/m2
    - Alcohol excess
    - Rapidly progressing to requiring insulin
    - Past history of DKA
    - Possibility of Latent Autoimmune Diabetes in Adults
    - Type 3 DM / pancreatic exocrine/endocrine dysfunction
- SGLT2i discontinued when patient develops DKA

Pre-treatment counselling

- Sick day rules
- Signs and symptoms of DKA
- Seek immediate medical help if symptoms DKA
- Avoid ketogenic diet and consider withholding SGLT2i if fasting
- Withold for 3 days prior to major surgical procedures (see peri-operative guidance for more information)
- Symptoms of hypovolaemia
- Temporarily withhold SGLT2i during acute illness
- Risks and symptoms of mycotic genital infection and self-care to maintain good genital hygiene (consider prophylactic anti-fungal if prior/recurrent infection)
- Symptoms of Fournier's gangrene (note MHRA warning)
- Discontinue during acute pyelonephritis or urosepsis
- Pregnancy and breast-feeding – avoid SGLT2i
- Foot disease and amputation risk – see below

Hypoglycaemia risk management

- Consider reducing dose insulin/sulphonylureas (SU)/meglitinides when initiating SGLT2i
- When initiating in people taking SUs (e.g. gliclazide) or meglitinides when HbA1c <58 mmol/mol AND eGFR >45 mL/min consider reducing dose SU or meglitinide by 50%
- When initiating SGLT2i in people taking insulin when HbA1c <58 mmol/mol AND eGFR >45 mL/min consider reducing insulin dose by 20%
- When initiating SGLT2i in people taking only metformin +/- pioglitazone +/- DPP-4i/gliptins or GLP-1RA, no dose adjustment necessary

Monitoring

- Early assessment of kidney function or potassium not indicated
- Early decline in eGFR is an expected drug effect
- Consider early clinical review and, if appropriate, a diuretic or antihypertensive dose reduction if considered at high risk of hypovolaemia
- Plan routine follow-up based on CKD stage including monitoring of bone parameters as appropriate for CKD stage

Cautions

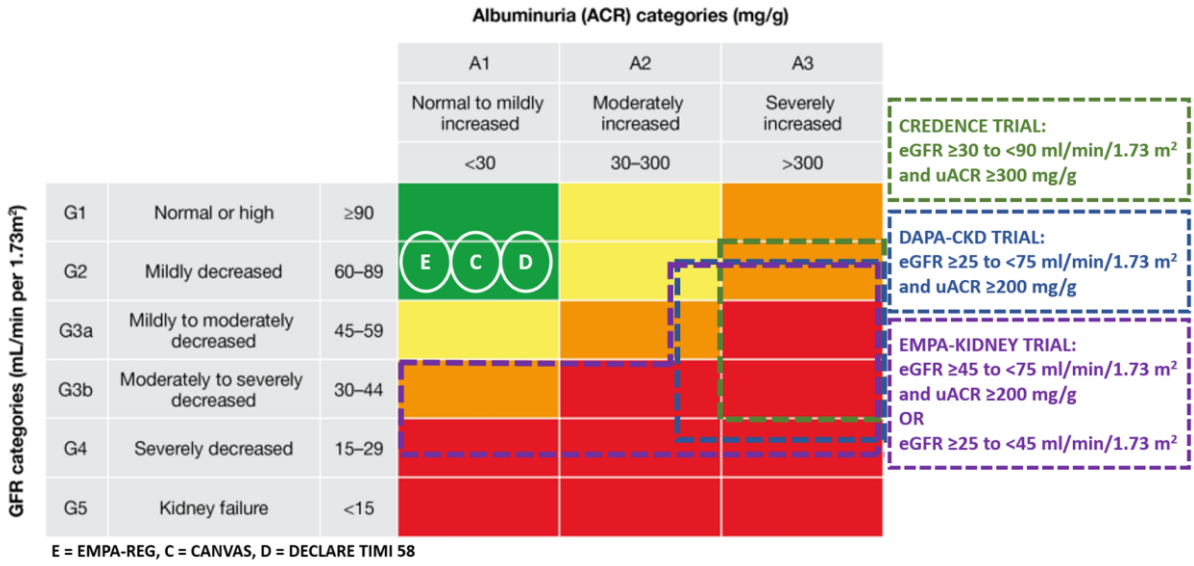
- The UK Kidney Association guideline suggests avoiding initiation in presence of active foot disease and withholding in those who develop foot complications
- Currently insufficient evidence on safety and efficacy to provide recommendation on SGLT2i in kidney transplant patients. Use in this group to treat diabetes should involve MDT discussion.

SGLT2i choice

Dapagliflozin, Canagliflozin, and Empagliflozin currently hold SMC approval for use for CKD indications (the relevant large outcome trials DAPA-CKD, CREDENCE, and EMPA-KIDNEY (respectively) are referenced at the end of this document).

The UKKA suggest that the beneficial effects of SGLT2i on kidney disease progression or risk of heart failure hospitalisation are likely to be a class effect. They recommend using SGLT2i with demonstrated efficacy for their given indications. This is summarised in the image below in terms of CKD stage.

Figure via NephJC, modified from Heerspink et al, NDT 2020
Note uACR>200 mg/g equivalent to uACR >23 mg/mmol



These and other SGLT2is are used for other indications (particularly diabetes and heart failure), and patients already established on an SGLT2i should not be switched to an alternative agent to treat their CKD.

This is an evolving therapeutic area with expanding indications and availability of other agents.

Dapagliflozin

Dapagliflozin 10mg daily can be initiated:

- in patients with an estimated glomerular filtration rate of ≥25 to ≤75 mL/min at treatment initiation, *and*
- are receiving an angiotensin converting enzyme inhibitor or angiotensin receptor blocker (unless these are not tolerated or contraindicated), *and*
- have a urine albumin creatinine ratio of at least 23mg/mmol, or type 2 diabetes mellitus *or* both

Dosing - Dapagliflozin 10mg once daily (consider using 5mg daily in patients with significant hepatic impairment).

Canagliflozin

Canagliflozin 100mg daily can be initiated if

- T2DM
- eGFR 30 mL/min – 90 mL/min
- ACR >30 mg/mmol

Dosing - Canagliflozin 100mg daily for CKD indication.
(300mg daily can be used for diabetes treatment when eGFR > 60ml/minute (should be reduced to 100mg/day if eGFR falls below 60ml/min)).

Empagliflozin

Empagliflozin 10mg daily can be initiated in patients having individually optimised standard care (including angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, unless these are contraindicated or not tolerated), and either, at the start of treatment:

- an estimated glomerular filtration rate (eGFR) of 20 mL/min up to 45 ml/min, or
- an eGFR of 45 mL/min up to 90 mL/min and either:
    - A urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more, or
    - Type 2 Diabetes Mellitus (T2DM).

Dosing – Empagliflozin 10mg for CKD indication

SGLTi withdrawal

SGLT2i should be stopped when patients commence Kidney Replacement Therapy (dialysis or transplant), or as otherwise indicated.

Pre-treatment evaluation

Patients should have baseline renal function and urine ACR performed in order to assess eligibility against criteria above. Imaging and consideration of kidney biopsy should proceed as usually indicated and are not necessary to exclude conditions such as polycystic kidney disease or vasculitis in order to initiate SGLT2i.

Audit / Evaluation of Response to Treatment

The overwhelming evidence base supporting use of these medicines is such that individual specific evaluation is not required.

References/Evidence

UK Kidney Association Clinical Practice Guideline: Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease, April 2023
https://guidelines.ukkidney.org/

SMC Dapagliflozin April 2022 SMC 2428
https://www.scottishmedicines.org.uk/medicines-advice/dapagliflozin-forxiga-full-smc2428/

NICE SGLT2i
https://cks.nice.org.uk/topics/diabetes-type-2/prescribing-information/sglt-2-inhibitors/

Executive summary of the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease: an update based on rapidly emerging new evidence
Rossing et al, Kidney International,Volume 102, Issue 5, 2022,Pages 990-999
https://doi.org/10.1016/j.kint.2022.06.013.

Dapagliflozin in Patients with Chronic Kidney Disease (DAPA CKD)
Heerspink et al, N Engl J Med 2020; 383:1436-1446

Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy (CREDENCE)
Perkovic et al, N Engl J Med 2019; 380:2295-2306

SGLT2i in Management of Chronic Kidney Disease, NHS GGC ADTC
https://ggcmedicines.org.uk/blog/medicines-update/sglt2i-in-management-of-chronic-kidney-disease-1/

Empagliflozin in Patients with Chronic Kidney Disease (EMPA-KIDNEY)
The EMPA-KIDNEY Collaborative Group, N Engl J Med 2023;388:117-127

Neph JC
https://www.nephjc.com/news/empa-kidney (accessed July 2026)

Heerspink HJL, et al. Rationale and protocol of the Dapagliflozin And Prevention of Adverse outcomes in Chronic Kidney Disease (DAPA-CKD) randomized controlled trial. Nephrol Dial Transplant. 2020 Feb 1;35(2):274-282. doi: 10.1093/ndt/gfz290. PMID: 32030417; PMCID: PMC7005525.

Appendices

1. Governance information for Guidance document

Lead Author(s):	Jack Fairweather
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Distribution	

CHANGE RECORD

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May 2022	Jack Fairweather	*Initial submission*	1
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