SGLT2 Inhibitor Cold Map

Indications for SGLT2i in CKD/Albuminuria/T2DM/ HFrEF/HFmrEF/HFpEF

				Albuminuria Categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥ 300mg/g ≥ 30mg/mmol
GFR Categories (ml/min/1.73m²) Description and range	**G1**	Normal to high	≥ 90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
			20			
	G5	Kidney failure	<15			

Cardiovascular / kidney risk reduction

Cardiovascular risk reduction only: HFrEF / HFmrEF / HFpEF

No evidence for benefit / safety*

** Benefits and safety to patients with a GFR less than 20, receiving dialysis or having a kidney transplant is under investigation.*

Indications for SGLT2i in CKD/Albuminuria/T2DM/ HFrEF/HFmrEF/HFpEF

	Indication	Class of recommendation	Level of evidence	Year
HFrEF (LVEF ≤ 40%)	Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A	ESC HF guidelines, 2021
	In patients with symptomatic chronic HFrEF, SGLT2 are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes.	I	A	AHA/ACC/HFSA Guidelines 2022
HFmrEF (LVEF 41–49%)	An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFmrEF to reduce the risk of HF hospitalization or CV death.	I	A	ESC HF guidelines update, 2023
	In patients with HFmrEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.	IIa	B-R	AHA/ACC/HFSA Guidelines 2022
HFpEF ≥50%	An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFpEF to reduce the risk of HF hospitalization or CV death.	I	A	ESC HF guidelines update, 2023
	In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.	IIa	B-R	AHA/ACC/HFSA Guidelines 2022
CKD	We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m2 with an SGLT2i.	I	A	KDIGO 2023
	We recommend treating adults with CKD with an SGLT2i for the following (1A): - eGFR ≥20 ml/min per 1.73 m2 with urine ACR ≥200 mg/g (≥20 mg/mmol), or - heart failure, irrespective of level of albuminuria.	I	A	KDIGO 2023
	We suggest treating adults with eGFR 20 to 45 ml/min per 1.73 m2 with urine ACR <200 mg/g (<20 mg/mmol) with an SGLT2i. The guidelines note the beneficial effects of SGLT2 inhibitors across a broad range of CKD patients, even in those without diabetes.	II	B	KDIGO 2023
TDM	Among individuals with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high cardiovascular risk, established kidney disease, or heart failure, a sodium–glucose cotransporter 2 inhibitor and/or glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular disease benefit is recommended as part of the glucose-lowering regimen and comprehensive cardiovascular risk reduction, independent of A1C and in consideration of person-specific factors.	I	A	Standard of care in diabetes (ADA) 2023 guidelines

Appendix

- KDIGO 2024 CLINICAL PRACTICE GUIDELINEFOR THE EVALUATION AND MANAGEMENT OF CHRONIC KIDNEY DISEASE
  - Chapter 3, Section 3.7 Sodium-glucose cotransporter-2 inhibitors (SGLT2i)
- KDIGO 2022 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE:
  - Page S19, S20 - for SGLT2i and eGFR criteria. Figure 1 | Kidney–heart risk factor management. Figure 2 | Holistic approach for improving outcomes in patients with diabetes and chronic kidney disease.
  - Page S22 - Figure 6 | Practical approach to initiating sodium-glucose cotransporter-2 inhibitors (SGLT2i) in patients with type 2 diabetes and chronic kidney disease (CKD).
  - Page S24, S75 - Practice Point 4.1:Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with both metformin and a SGLT2i, and additional drug therapy as needed for glycemic control (Figure 23).
  - Page S24 - Practice Point 4.2: Most patients with T2D, CKD, and eGFR ǂ 30ml/min per 1.73m2 would benefit from treatment with both metformin and an SGLT2i.
  - Page S76 - (Trials) Figure 24 | Overview of select large, placebo-controlled clinical outcome trials assessing the benefits and harms of SGLT2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors.
  - Page S43-45 - Empa-kidney for albuminuria cut-off ≥20 mg/mmol. CREDENCE (30 mg/ml/1.73 m3) and DAPA-CKD (>25 mg/ml/1.73) and EMPA-Kidney (20 mg/ml/1.73m3).
  - Page S38 - Recommendation1.3.1:We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min/1.73m2 with an SGLT2i.
- Task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC).
  - 5.1.1 SGLT2i are recommended in patients with CKD and T2DM, and with additional characteristics including an eGFR >20–25 mL/min/1.73 m2, to reduce the risk of HF hospitalization or CV death.
- ADA - Standards of Medical care in diabetes 2022.
  - Recommendations 11.3a For patients with type 2 diabetes and DKD, use of an SGLT2 inhibitor in patients with an eGFR ≥20 mL/min/1.73 m^2 and urinary albumin ≥300 mg/g creatinine is recommended to reduce CKD progression and CV events.
  - 11.3b In patients with type 2 diabetes and CKD, consider use of SGLT2 inhibitors additionally for CV risk reduction when eGFRand urinary albumin creatinine are ≥25 mL/min/1.73 m^2 or ≥300 mg/g, respectively.
- More research is needed to evaluate the cardiorenal outcomes and complications of SGLT2i therapy in glomerular diseases & tra nsplant.

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