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	60-90			
	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 ‡ 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 eGFR and 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 & transplant.

References

- 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines Paul A. Heidenreich, MD, MS, FACC, FAHA, FHFSA, Chair, Biykem Bozkurt, MD, PhD, FACC, FAHA, FHFSA, Vice Chair, David Aguilar, MD, MSc, FAHA, Larry A. Allen, MD, MHS, FACC, FAHA, FHFSA, Joni J. Byun, Monica M. Colvin, MD, MS, FAHA, Anita Deswal, MD, MPH, FACC, FAHA, FHFSA, Mark H. Drazner, MD, MSc, FACC, FAHA, FHFSA, Shannon M. Dunlay, MD, MS, FAHA, FHFSA, Linda R. Evers, JD, James C. Fang, MD, FACC, FAHA, FHFSA, Savitri E. Fedson, MD, MA, Gregg C. Fonarow, MD, FACC, FAHA, FHFSA, Salim S. Hayek, MD, FACC, Adrian F. Hernandez, MD, MHS, Prateeti Khazanie, MD, MPH, FHFSA, Michelle M. Kittleson, MD, PhD, Christopher S. Lee, PhD, RN, FAHA, FHFSA, Mark S. Link, MD, Carmelo A. Milano, MD, Lorraine C. Nnacheta, DrPH, MPH, Alexander T. Sandhu, MD, MS, Lynne Warner Stevenson, MD, FACC, FAHA, FHFSA, Orly Vardeny, PharmD, MS, FAHA, FHFSA, Amanda R. Vest, MBBS, MPH, FHFSA, Clyde W. Yancy, MD, MSc, MACC, FAHA, FHFSA
- 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC
- American Diabetes Association; *Standards of Medical Care in Diabetes—2022* Abridged for Primary Care Providers. *Clin Diabetes* 1 January 2022; 40 (1): 10–38. https://doi.org/10.2337/cd22-as01
- Clara García Carro, Andrea Bedia Raba, Eduardo J Banegas Deras, Luis Alberto Vigara, Rosalía Valero San Cecilio, Leónidas Cruzado Vega, Eva Gavela, García M Elena González, Isabel Pérez-Flores, Francisco Sanchez-Bielsa, FC 116: SGLT2 Inhibitors in Kidney Transplantation: A Multicenter Study, *Nephrology Dialysis Transplantation*, Volume 37, Issue Supplement_3, May 2022, gfac124.001, https://doi.org/10.1093/ndt/gfac124.001
- GLOMCON MINI REVIEW| VOLUME 5, ISSUE 4, 100608, APRIL 2023. Sodium Glucose Cotransporter 2 (SGLT2) Inhibitors and CKD: Are You a #Flozinator? Anoushka Krishnan, Mythri Shankar, Edgar V. Lerma, Nasim Wiegley on behalf of theGlomCon Editorial Team. January 31, 2023DOI:https://doi.org/10.1016/j.xkme.2023.100608
- KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases
- KDIGO 2022 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANAGEMENT IN CHRONIC KIDNEY DISEASE.
- KDIGO 2024 CLINICAL PRACTICE GUIDELINE FOR THE EVALUATION AND MANAGEMENT OF CHRONIC KIDNEY DISEASE
- McQuarrie, Emily P.a; Gillis, Keith A.a; Mark, Patrick B.a,b. Seven suggestions for successful SGLT2i use in glomerular disease - a standalone CKD therapy?. Current Opinion in Nephrology and Hypertension 31(3):p 272-277, May 2022. | DOI: 10.1097/MNH.0000000000000786
- Theresa A McDonagh, Marco Metra, Marianna Adamo, Roy S Gardner, Andreas Baumbach, Michael Böhm, Haran Burri, Javed Butler, Jelena Čelutkienė, Ovidiu Chioncel, John G F Cleland, Maria Generosa Crespo-Leiro, Dimitrios Farmakis, Martine Gilard, Stephane Heymans, Arno W Hoes, Tiny Jaarsma, Ewa A Jankowska, Mitja Lainscak, Carolyn S P Lam, Alexander R Lyon, John J V McMurray, Alexandre Mebazaa, Richard Mindham, Claudio Muneretto, Massimo Francesco Piepoli, Susanna Price, Giuseppe M C Rosano, Frank Ruschitzka, Anne Kathrine Skibelund, ESC Scientific Document Group, 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 44, Issue 37, 1 October 2023, Pages 3627–3639, https://doi.org/10.1093/eurheartj/ehad195
- VOLUME 7, ISSUE 7, P1463-1476, JULY 2022, Prescribing SGLT2 Inhibitors in Patients With CKD: Expanding Indications and Practical Considerations. Kevin Yau, Atit Dharia, Ibrahim Alrowiyti, David Z.I. Cherney, May 05, 2022DOI:https://doi.org/10.1016/j.ekir.2022.04.094
- Wheeler DC, Toto RD, Stefánsson BV, Jongs N, Chertow GM, Greene T, Hou FF, McMurray JJV, Pecoits-Filho R, Correa-Rotter R, Rossing P, Sjöström CD, Umanath K, Langkilde AM, Heerspink HJL; DAPA-CKD Trial Committees and Investigators. A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. Kidney Int. 2021 Jul;100(1):215-224. doi: 10.1016/j.kint.2021.03.033. Epub 2021 Apr 18. PMID: 33878338.

For funding and support information, see: https://www.theisn.org/initiatives/toolkits/sglt2i-toolkit/#Support