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CADTH Reference List

Dapagliflozin for Chronic Kidney Disease Guidelines

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Summary of Abstracts

CADTH

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Key Message

- No relevant evidence-based guidelines were identified describing recommendations for best practice regarding the use of dapagliflozin for the treatment of adults with chronic kidney disease.

Research Question

What are the evidence-based guidelines regarding the use of dapagliflozin for the treatment of adults with chronic kidney disease?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were dapagliflozin and chronic kidney disease. No filters were applied to limit the retrieval by study type. Conference abstracts were removed from the search results. The search was also limited to English language documents published between Jan 1, 2016 and Dec 11, 2021.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications. Open access full-text versions of evidence-based guidelines were reviewed when available, and relevant recommendations were summarized.

Table 1: Selection Criteria

Criteria	Description
Population	Adults with chronic kidney disease
Intervention	Dapagliflozin (Forxiga) 5 mg and 10 mg oral tablets
Comparator	Not applicable
Outcomes	Recommendations for best practice regarding the use of dapagliflozin for the treatment of adults with chronic kidney disease (e.g., appropriate patient populations or clinical settings, recommended treatment strategies, strategies to mitigate harms, adverse events, and misuse)
Study designs	Evidence-based guidelines

mg = milligram

Results

No relevant evidence-based guidelines were identified describing recommendations for best practice regarding the use of dapagliflozin for the treatment of adults with chronic kidney disease.

References of potential interest that did not meet the inclusion criteria but provided guidance and recommendations related to the use of dapagliflozin or non-specific sodium glucose co-transporter 2 (SGLT2) inhibitors for the treatment of adults with chronic kidney disease are summarized in Appendix 1. Other articles of potential interest are provided in Appendix 2.

Overall Summary of Findings

No eligible evidence-based guidelines were identified describing recommendations for best practice regarding the use of dapagliflozin for the treatment of adults with chronic kidney disease; therefore, no summary can be provided.

References

Guidelines and Recommendations

No eligible evidence-based guidelines were identified.

Appendix 1: Summary of Identified Recommendations

The following publications either did not meet the methodological criteria to be considered an evidence-based guideline,[1] or did not specify dapagliflozin within the recommendations[2-4] and therefore were not eligible for inclusion in the main body of this report.

Nonetheless, these 4 publications contained guidance and/or recommendations that bore some relevance to the use of dapagliflozin in patients with chronic kidney disease (CKD), but were excluded from the review due to their ineligibility (as above). Of note, a fifth publication was also identified from the National Institute for Health and Care Excellence (NICE) in the UK, which describes relevant guidance that remains under development as of the publication of this report, and is therefore not yet published thus, was neither eligible for inclusion in this review, nor for the summary provided in this Appendix; the reference is noted below in Appendix 2 for information.[6]

One of the relevant publications is a position paper that is broader in scope than the current review i.e., the focus is on SLGT2 inhibitors in general for the treatment of Type II diabetes (T2D) and/or heart failure. Nonetheless, the paper did put forward several recommendations — one of which is relevant to dapagliflozin in chronic kidney disease and recommends its use (as well as that of canagliflozin, which was not relevant to the current review) in patients with T2D and CKD to prevent hospitalization for HF.[1] The recommendation also confirms the safety and efficacy of both SGLT2 inhibitors in patients with and without T2D.[1] However, because this position paper does not specify a comprehensive literature review or systematic method for developing its recommendations, it is not eligible for inclusion in this review, which sought evidence-based guidelines only.

Two of the publications are clinical practice guidelines;[2,3] 1 from the UK Kidney Association (UKKA)[2] and another from Kidney Disease Improving Global Outcomes (KDIGO).[3] Both clinical practice guidelines demonstrated the use of a systematic approach to consulting the literature and developing recommendations, and provided guidance specific to CKD; however, the recommendations put forward were not specific to dapagliflozin, and rather addressed the use of SGLT2 inhibitors, more generally.[2,3] The UKKA guideline presented several recommendations in support of initiating treatment with SGLT2 inhibitors in patients with CKD (with or without T2D), as well as guidance for implementing SGLT2 inhibitors in clinical practice.[2] Similarly, the recommendations presented in the KDIGO guidelines were broader in scope than the eligibility criteria for this review i.e., most were not specific to SGLT2 inhibitors, and 1 recommendation that did address the use of SGLT2 inhibitors did not specify information particular to dapagliflozin.[3] Nonetheless, the 1 recommendation addressing SGLT2 inhibitors did support its use in patients with CKD and T2D, provided the patients also have an estimated glomerular filtration rate (eGFR) of ≥30 ml/min per 1.73 m^2.[3]

Finally, a Consensus Statement from the Working Group of the Endocrine Society of Bengal was identified, which puts forth several evidence-based recommendations for the use of SGLT2 inhibitors in patients with CKD and T2D, specifically patients with diabetic kidney disease (DKD).[4] Similar to the other relevant but ineligible publications identified in this review, the Consensus Statement puts forward several recommendations in favour of the use of SGLT2 inhibitors to support the prevention of progressive DKD, as well as recommendations to support the implementation of SGLT2 inhibitors into clinical practice.[4]

Guidelines and Recommendations

Methodology Not Specified

1. Gronda, E., et al. ANMCO POSITION PAPER: on administration of type 2 sodium-glucose co-transporter inhibitors to prevent heart failure in diabetic patients and to treat heart failure patients with and without diabetes. Eur Heart J. 2021;23(Suppl C): C184-C195.

   BACKGROUND: This ANMCO (Associazione Nazionale Medici Cardiologi Ospedalieri) position paper aims to analyse the complex action of sodium-glucose co-transporter 2 inhibitors at the level of the kidney and cardiovascular system, focusing on the effect that these molecules have shown in the prevention and treatment of heart failure in diabetic and non-diabetic subjects. The goal was pursued by comparing the data generated with pathophysiology studies and with multicentre controlled studies in large populations. In accordance with the analysis carried out in the document, the following recommendations are issued: (i) canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin are molecules recommended for the prevention of heart failure hospitalizations in type 2 diabetic subjects; (ii) canagliflozin and dapagliflozin are recommended for the prevention of heart failure hospitalizations in type 2 diabetic subjects with severe chronic kidney disease, dapagliflozin proved to be safe and

effective also in diabetic subjects; and (iii) dapagliflozin and empagliflozin are recommended to reduce the combined risk of heart failure and cardiovascular death in diabetic and non-diabetic subjects with heart failure and reduced ejection fraction.

See: Recommendation (2) on page C194.

Recommendations Not Specific to Dapagliflozin

2. UK Kidney Association.UK Kidney Association Clinical Practice Guideline: Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease; 2021. https://ukkidney.org/sites/renal.org/files/UKKA%20guideline_SGLT2i%20in%20adults%20with%20kidney%20disease%20v1%2020.10.21.pdf Accessed 23 Dec 2021.

SUMMARY: Prevention of kidney disease progression and reducing cardiovascular risk are unmet clinical needs among people with chronic kidney disease (CKD). Large-scale placebo-controlled trials have demonstrated that sodium-glucose co-transporter-2 (SGLT-2) inhibition favourably modifies both such risks in a range of different studied populations. In people with CKD, the CREDENCE and DAPA-CKD trials have demonstrated SGLT-2 inhibition's particular efficacy at reducing risk of kidney disease progression in people with type 2 diabetes mellitus (DM) and albuminuric diabetic kidney disease. Subgroup analyses from DAPA-CKD also suggest these benefits extend to certain types of albuminuric CKD, irrespective of the presence of DM. This section provides the background to this guideline by introducing: (i) CKD and the concept of intraglomerular hypertension; (ii) the molecular mechanisms of SGLT-2 inhibition; and (iii) the large placebo-controlled trials that have informed us of its cardio-renal beneficial effects.

See: Summary of Recommendations on pages 5 to 8.

3. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2020;98: S1-S115.

ABSTRACT: The Kidney Disease: Improving Global Outcomes (KDIGO) 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease (CKD) represents the first KDIGO guideline on this subject. The scope includes topics such as comprehensive care, glycemic monitoring and targets, lifestyle and antihyperglycemic interventions, and approaches to self-management and optimal models of care. The goal of the guideline is to generate a useful resource for clinicians and patients by providing actionable recommendations with infographics based on a rigorous, formal systematic literature review. Another aim is to propose research recommendations for areas in which there are gaps in knowledge. The guideline targets a broad audience of clinicians treating diabetes and CKD while taking into account implications for policy and payment. The development of this guideline followed an explicit process of evidence review and appraisal. Treatment approaches and guideline recommendations are based on systematic reviews of relevant studies, appraisal of the quality of the evidence, and the strength of recommendations following the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Limitations of the evidence are discussed and areas for future research are presented.

See: Recommendation 4.2.1 on page S27.

4. Roy, A., et al. Kidney Disease in Type 2 Diabetes Mellitus and Benefits of Sodium-Glucose Cotransporter 2 Inhibitors: A Consensus Statement. Diabetes Ther. 2020;11(12): 2791-2827.

ABSTRACT: Diabetic kidney disease (DKD) occurs in approximately 20–40% of patients with type 2 diabetes mellitus. Patients with DKD have a higher risk of cardiovascular and all-cause mortality. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and antihyperglycemic drugs form the mainstay of DKD management and aim to restrict progression to more severe stages of DKD. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) control hyperglycemia by blocking renal glucose reabsorption in addition to preventing inflammation, thereby improving endothelial function and reducing oxidative stress; consequently, this class of prescription medicines is emerging as an important addition to the therapeutic armamentarium. The EMPAREG OUTCOME, DECLARE TIMI 58, and CANVAS trials demonstrated the renoprotective effects of SGLT2i, such as restricting decline in glomerular filtration rate, in the progression of albuminuria, and in death due to renal causes. The renoprotection provided by SGLT2i was further confirmed in the CREDENCE study, which showed a 30% reduction in progression of chronic kidney disease, and in the DELIGHT study, which demonstrated a reduction in albuminuria with dapagliflozin compared with placebo (- 21.0%, confidence interval [CI] -34.1 to - 5.2, p = 0.011). Furthermore, a meta analysis demonstrated a reduced risk of dialysis, transplantation, or death due to kidney disease (relative risk 0.67; 95% CI 0.52–0.86; p = 0.0019) and a 45% risk reduction in worsening of renal function, end-stage renal disease, or renal death (hazard ratio 0.55, CI 0.48–0.64, p\0.0001) with SGLT2i, irrespective of baseline estimated glomerular filtration rate. Thus, there is emerging evidence that SGLT2i may be used to curb the mortality and improve the quality of life in patients with DKD. However, clinicians need to effectively select candidates for SGLT2i therapy. In this consensus statement, we have qualitatively synthesized evidence

demonstrating the renal effects of SGLT2i and proposed recommendations for optimal use of SGLT2i to effectively manage and delay progression of DKD.

See: Recommendations Table on pages 2820-1.

Appendix 2: Additional References

Related CADTH Reports

5. Khangura SD, Severn M. Dapagliflozin for Chronic Kidney Disease. *CADTH Health Technology Review*. Ottawa: CADTH; Feb 2022. https://www.cadth.ca/

Guidelines and Recommendations

Guideline in Development

6. NICE. Dapagliflozin for treating chronic kidney disease (ID3866); [in development]. https://www.nice.org.uk/guidance/indevelopment/gid-ta10808/documents Accessed 23 Dec 2021.