



CADTH Reimbursement Recommendation

Dapagliflozin

Reimbursement request: Dapagliflozin for the treatment of chronic kidney disease in adults, with or without diabetes mellitus, to reduce the risk of sustained estimated glomerular filtration rate decline, end-stage kidney disease, and cardiovascular and renal death.

Final recommendation: Reimburse with conditions

Summary of CADTH Recommendation

The CADTH Formulary Management Expert Committee (FMEC) concluded there was an unmet need to reduce the progression of chronic kidney disease (CKD), especially for those patients without diabetes, given the lack of reimbursed options.

Evidence from the DAPA-CKD trial, the largest trial with the longest follow-up identified by a systematic review, demonstrated that patients with CKD treated with dapagliflozin had a slower decline of estimated glomerular filtration rate, a reduction in the urinary albumin to creatinine ratio, and increased time to cardiovascular and renal events compared with placebo.

FMEC concluded that reimbursement should be restricted to patients eligible for the DAPA-CKD trial, which included meeting diagnostic criteria for CKD and treatment with an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker at the maximum-tolerated dose.

What Is Chronic Kidney Disease?

Chronic kidney disease (CKD) is abnormalities of kidney structure and/or function, for over 3 months, leading to a gradual loss of kidney function. CKD is classified based on cause, glomerular filtration rate, and albuminuria level. It is the leading cause of kidney failure in patients and will ultimately require dialysis or kidney transplant. In Canada, the prevalence rate is approximately 12%.

What Did We Hear From Patients?

CKD impacts patients' quality of life, ability to work, engagement in physical activity, and lifestyle. Access to treatment, need for several medications, and time needed off work for treatment are challenges with current therapies. Affordable options are needed to improve energy levels and quality of life and reduce hospital visits.



Refer to [Patient Group Input](#) section of the CADTH report.

What Did We Hear From Clinicians?

Clinicians reported current therapies do not reliably delay disease progression and more effective therapies are needed. They noted the goal of therapy is to prolong dialysis-free life and improve quality of life. Clinicians indicated patients who meet the DAPA-CKD trial inclusion criteria are suitable for dapagliflozin treatment.



Refer to [Clinician Input](#) section of the CADTH report.

What Did We Hear From Industry and Public Drug Programs?

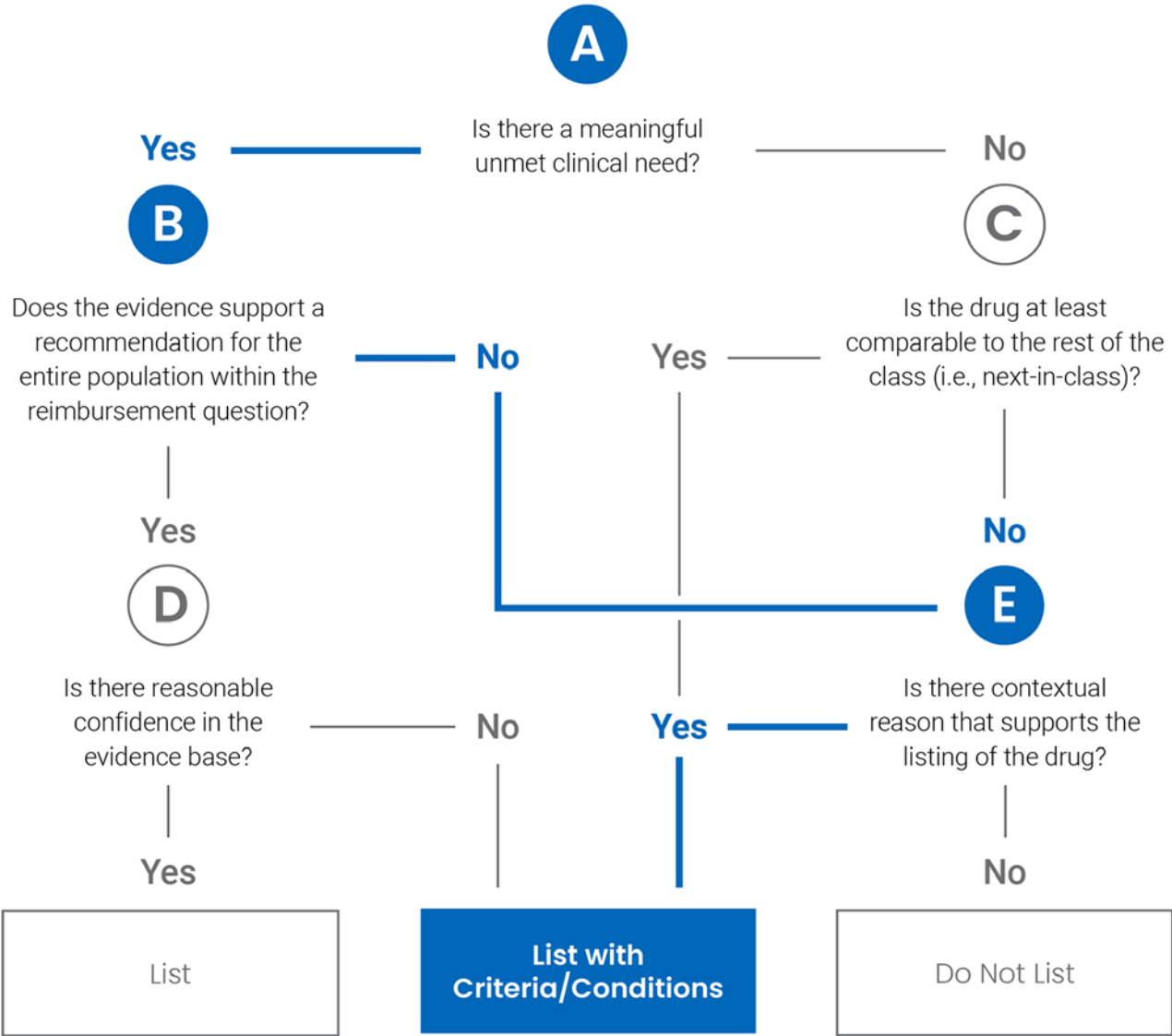
Industry described the burden and impact on patients living with CKD and highlighted the importance of protecting patients from negative outcomes. Public drug plans questioned the appropriate time to initiate therapy, treatment with prior therapies and standard of care, continuation and renewal criteria, and appropriate prescribers.



Refer to [Industry Input](#) and [Drug Plan Input](#) sections of the CADTH report.

Deliberative Framework

Figure 1: Decision Path



Decision Summary

Table 1: Why Did FMEC Make This Recommendation?

Decision node	Vote	Reason
(A) Is there a meaningful unmet clinical need?	Yes (6)	- FMEC considered that a treatment gap exists in patients with CKD without T2DM on SOC (ACE inhibitors or ARBs) with residual risk and these patients would benefit from treatment with dapagliflozin for renal and cardiovascular outcomes and reducing the progression of CKD. - FMEC noted that finerenone is a potential option for patients with CKD and T2DM; however, an unmet need still exists for patients without T2DM. The committee noted there is an evidence gap in comparative efficacy of dapagliflozin and finerenone.
	No (1)	- FMEC considered that there may be drugs within the same class as dapagliflozin (i.e., other SGLT2 inhibitors) that may achieve similar benefits; however, their comparative effectiveness for CKD is uncertain. - FMEC acknowledged evidence of other drugs within the class of SGLT2 inhibitors are emerging.
(B) Does the evidence support a recommendation for the entire population within the reimbursement question? Population under consideration for reimbursement: Adults with CKD with or without T2DM	Yes (0)	—
	No (7)	- FMEC noted that, in the DAPA-CKD trial, patients with certain etiologies of CKD were excluded, such as those with polycystic kidney disease or autoimmune disease taking immunosuppressive therapy. Patients already receiving a SGLT2 inhibitor were also excluded. - FMEC concluded there is insufficient evidence to support a recommendation for the entire population of patients with CKD beyond the DAPA-CKD trial population, but would benefit a subset of the population based on the trial inclusion and exclusion criteria.
(E) Is there a subpopulation or contextual reason that supports the reimbursement of the drug?	Yes (7)	- FMEC noted that evidence provided by the DAPA-CKD trial supports that dapagliflozin is beneficial when used as an add-on therapy to SOC for important renal outcomes (i.e., development of ESKD, doubling of serum creatinine, and decline in eGFR). FMEC highlighted that certainty in the evidence is limited to those patients who met the inclusion criteria of DAPA-CKD. - FMEC acknowledged that the DAPA-CKD trial demonstrated a benefit of dapagliflozin on the composite outcomes (i.e., primary outcome was time to 50% or greater eGFR decline, ESKD, cardiovascular death, or renal death), of which 197 of 2,152 (9.2%) patients in the dapagliflozin group and 312 of 2,152 (14.5%) patients in the placebo group experienced a component of the composite outcomes (HR = 0.61; 95% CI, 0.51 to 0.72; P < 0.001).
	No (0)	—

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; CI = confidence interval; CKD = chronic kidney disease; DM = diabetes mellitus; ESKD = end-stage kidney disease; FMEC = CADTH Formulary Management Expert Committee; HR = hazard ratio; SGLT2 = sodium-glucose cotransporter-2; SOC = standard of care; T2DM = type 2 diabetes mellitus.

Full Recommendation

FMEC recommends that dapagliflozin be reimbursed for adult patients with CKD, with or without T2DM, if the conditions presented in [Table 2](#) are met.

Table 2: Reimbursement Conditions, Reasons, and Guidance

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Dapagliflozin should be reimbursed in patients who meet the diagnostic criteria for CKD (eGFR 25 mL/minute/1.73 m ² to 75 mL/minute/1.73 m ²) with a UACR of 200 mg/g to 5,000 mg/g and treated with an ACE inhibitor or ARB at the maximum-tolerated dose.	Initiation criteria reflect the enrolment criteria for the DAPA-CKD trial (eGFR of 25 mL/minute/1.73 m² to 75 mL/minute/1.73 m² and a UACR of 200 mg/g to 5,000 mg/g) and is reflective of clinical practice in Canada and standard of care, as per clinical practice guidelines. In DAPA-CKD, all participants were required to be receiving a stable dose of an ACE inhibitor or ARB for at least 4 weeks. Of the 2,152 participants in the dapagliflozin arm, 673 of (31.3%) and 1,444 (67.1%) were on an ACE inhibitor and ARB, respectively. Benefits from dapagliflozin for patients with CKD with lower proteinuria (i.e., UACR < 200 mg/g) is unclear and remains an evidence gap.	Patients whose CKD is caused by polycystic kidney disease or autoimmune conditions managed with immunosuppressants should not receive dapagliflozin because there are no data on efficacy or safety in these patients. Patients who are already taking an SGLT2 inhibitor for glycemic control or because of risk of heart failure do not necessarily require switching to dapagliflozin to prevent the progression of renal disease. If clinically indicated, patients with CKD and diabetes may take dapagliflozin in combination with finerenone for preservation of renal status. Contraindication or intolerance to an ACE inhibitor or ARB does not preclude a patient from receiving dapagliflozin for CKD; however, this remains an evidence gap.
Discontinuation		
2. Patients whose renal function deteriorates to stage 5 ESRD, who begin dialysis or undergo renal transplant, and who are prescribed dapagliflozin solely for CKD should discontinue dapagliflozin.	Dapagliflozin is contraindicated in patients who are undergoing dialysis. Evidence for the benefit of dapagliflozin for patients who are at later stages of renal disease is unknown.	—
Prescribing		
3. Dapagliflozin may be prescribed by appropriate specialists or by family physicians for the purposes of reducing renal function deterioration.	Based on clinical expert opinion, it would be appropriate for primary care clinicians to prescribe dapagliflozin.	—

Reimbursement condition	Reason	Implementation guidance
Cost		
4. Dapagliflozin should not be priced higher than any other SGLT2 inhibitor (including generic agents as they become available).	No comparative evidence to suggest superiority.	—

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; SGLT2 = sodium-glucose cotransporter-2; UACR = urinary albumin to creatine ratio.

Feedback on Draft Recommendation

CADTH did not receive feedback from stakeholders.

FMEC Information

Members of the committee: Dr. Emily Reynen (Chair), Dr. Alun Edwards, Ms. Valerie McDonald, Dr. Jim Silviu, Dr. Marianne Taylor, Dr. Maureen Trudeau, Dr. Dominika Wranik, Dr. Swapnil Hiremath (guest specialist)

Meeting date: June 29, 2023

Conflicts of interest: None

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