CADTH

CADTH Reimbursement Review

CADTH Reimbursement Recommendation

(Draft)

Finerenone (Kerendia)

Indication: KERENDIA (finerenone) is indicated as an adjunct to standard of care therapy in adults with chronic kidney disease (CKD) and type 2 diabetes (T2D) to reduce the risk of:

- End-stage kidney disease and a sustained decrease in estimated glomerular filtration rate,
- Cardiovascular death, non-fatal myocardial infarction and hospitalization for heart failure.

Sponsor: Bayer Inc.

Recommendation: Reimburse with Conditions

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CADTH

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Recommendation

The CADTH Canadian Drug Expert Committee (CDEC) recommends that finerenone be reimbursed as an adjunct to standard of care therapy in adults with chronic kidney disease (CKD) and type 2 diabetes (T2D) to reduce the risk of end-stage kidney disease (ESKD) and a sustained decrease in estimated glomerular filtration rate (eGFR), and cardiovascular death, non-fatal myocardial infarction and hospitalization for heart failure only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

Two randomized, double-blind, active-controlled, phase III trials (FIDELIO, N=5734; FIGARO, N=7437) in adult patients with CKD and T2D demonstrated that when added to standard of care, treatment with finerenone was associated with a statistically significant reduction in the risk of ESKD in FIDELIO trial and cardiovascular (CV) events compared to placebo plus standard of care. The primary outcome in the FIDELIO trial was the time to the first occurrence of the 40% renal composite endpoint, and the primary objective of FIGARO was the time to first occurrence of the cardiac composite endpoint. The first secondary outcome in each trial was the primary outcome of the other trial. In the FIDELIO trial, after 36 months of treatment, finerenone was associated with a 17.5% risk reduction in the time to the first occurrence of the 40% renal composite endpoint, and the hazard ratio (HR) was 0.825 (95% CI 0.73 to 0.93, p-value =0.0014) in favor of finerenone. In the FIGARO trial, after 48 months of treatment, the HR for this endpoint occurred was 0.87 (95% CI 0.76 to 1.01, p-value =0.0689) which was not statistically significant. In the FIDELIO trial, finerenone was associated with a 14% risk reduction in the time to first occurrence of the cardiac composite endpoint, and the HR was 0.86 (95% CI 0.75 to 0.99, p-value = 0.0339) in favor of finerenone, while in FIGARO, finerenone was associated with a 13% risk reduction, and the HR was 0.87 (95% CI 0.76 to 0.98, p-value = 0.0264) in favor of finerenone. CDEC noted that in the FIDELIO and FIGARO trials, 100% of patients in both arms of both trials were receiving either an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) as part of standard of care therapy, but only 6.7% of patients enrolled received sodium-glucose co-transporter-2 inhibitors (SGLT2is) as part of standard of care therapy. Due to the uncertainty around the efficacy and safety of adding finerenone to a standard of care therapy that includes ACEi or ARB in combination with an SGLT2i, CDEC recommended that finerenone be reimbursed only in patients who are not receiving SGLT2i.

Patients and clinical experts identified a need for treatment options that reduce the risk of progression to kidney failure and cardiovascular events and improve health-related quality of life (HRQoL). CDEC concluded that based on the evidence, finerenone appears to address some of the needs identified by patients by reducing the risk of progression to kidney failure and cardiovascular events; however, no definitive conclusions could be made regarding the effects of finerenone on the improvement of HRQoL.

Given the structure of the submitted economic model, CADTH could not produce a base case estimation of the cost-effectiveness of finerenone; therefore, CDEC considered exploratory reanalyses conducted by CADTH which considered the cost-effectiveness of finerenone relative to standard of care (SoC) utilizing different assumptions. Based on the sponsor's submitted price for finerenone and publicly listed prices for all other drug costs, the incremental cost-effectiveness ratio (ICER) ranged from $70,052 to $2,994,490 per quality-adjusted life-year (QALY). The presence of a cardiovascular mortality benefit alongside the degree of dialysis reduction had the largest impact on the results. In all reanalyses price reductions would be required for finerenone to achieve an ICER of $50,000 per QALY.

Table 1. Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Patients with CKD and T2D who have an eGFR level of at least 25 mL/min/1.73 m^2 and albuminuria level of at least 30mg/g (or 3 mg/mmol)	At least 97% of the patients enrolled in the FIDELIO and FIGARO trials had eGFR level of at least 25 mL/min/1.73 m^2 and albuminuria level of at least 30mg/g.	—
2. Patients must be receiving maximally tolerated doses of ACEi or ARB therapy	All patients in FIDELIO and FIGARO studies were on a maximal tolerated dose of ACEi or ARB as standard of care.	—
3. Treatment with finerenone must not be reimbursed in patients: 3.1. with CHF NYHA class II-IV or 3.2. receiving a MRA or 3.3. receiving a SGLT2i regardless of indication	Patients with clinical diagnosis of chronic heart failure with reduced ejection fraction and persistent symptoms (NYHA class II – IV) at the run-in visit were excluded from the FIDELIO and FIGARO trials. Patients who could not discontinue their MRA treatment at least 4 weeks prior to the screening visit were excluded from the FIDELIO and FIGARO trials. There is limited data to support the efficacy and safety of combination finerenone and SGLT2i therapy, as only 6.7% of patients were using SGLT2i therapy at baseline in the FIDELIO and FIGARO trials.	—
Discontinuation		
4. Treatment with finerenone must be discontinued if the patient progresses to ESKD requiring dialysis or transplant	Patients with ESKD were excluded from the FIDELIO and FIGARO trials; no evidence for the use of finerenone in patients who progress to ESKD was identified.	—
Pricing		
5. A reduction in price	Based on the exploratory reanalyses presented, the committee felt that a price reduction of at least 55% would be needed to improve the probability that finerenone is cost effective at a $50,000 per QALY threshold. This was due to uncertainties with expected mortality benefits and the degree of dialysis reduction seen from finerenone relative to SoC. As outstanding uncertainty remains it was noted that higher price reductions may be required.	—
Feasibility of adoption		

Reimbursement condition	Reason	Implementation guidance
6. The feasibility of adoption of finerenone must be addressed	At the submitted price, the budget impact of finerenone is expected to be greater than $40 million in years 2 and 3 if funded for all patients with CKD and T2DM, regardless of what treatments are included in standard of care. In the proposed population outlined by CDEC; patients would not receive finerenone if they were on an SGLT2i as part of their standard of care. The budget impact in this population is uncertain.	—

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CHF = chronic heart failure; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association; SGLT2is = sodium-glucose co-transporter-2 inhibitors; T2D = type 2 diabetes.

Discussion Points

- CDEC remained uncertain regarding the generalizability of results from the pivotal studies to patients who would receive finerenone as an add on to ACEi or ARB, and a SGLT2i. Although clinical experts noted that finerenone would be an adjunct to standard of care therapy that includes ACEi or ARBs, and SGLT2i, and that SGLT2i were recently added to the guidelines for managing patients with CKD and T2D, only 6.7% of patients enrolled in the FIDELIO and FIGARO trials were treated with SGLT2i at baseline. CDEC discussed that due to the limited evidence it is unknown what added benefit finerenone would provide to patients who are also receiving SGLT2i therapy; likewise, the safety of this combination is unknown.
- The direct comparison of finerenone and SGLT2i is limited by the small subpopulation included in the trials. A network meta-analysis (NMA) that compared finerenone and SGLT2i in patients with CKD and T2D with background treatment that included ACEi or ARB concluded that SGLT2i are more effective than finerenone at reducing kidney function progression and hospitalization due to heart failure events in this population. However, only 1 trial out of the included 8 trials assessed finerenone which limited the statistical power of this NMA, and precluded drawing definitive conclusions about the comparative effectiveness of finerenone versus SGLT2i.
- The FIDELIO and FIGARO trials were not powered to assess the risk of all-cause mortality and all-cause hospitalization; therefore, the effect of finerenone on these outcomes remains unknown.
- CDEC discussed that there was inconsistency in the results of the 40% renal composite outcome between FIDELIO and FIGARO trials and noted that the FIDELIO trial enrolled patients who had worse characteristics of CKD at baseline (lower eGFR and higher UACR) than those enrolled in the FIGARO trial. In the FIDELIO trial, the mean baseline eGFR was approximately 44 mL/min/1.73 m^2 (SD 12.5) in both groups, and the mean baseline UACR was 798.8 mg/g (SD 2.7) and 814.7 mg/g (SD 2.7) in the finerenone and placebo groups respectively, while in FIGARO, the mean baseline eGFR was approximately 68 mL/min/1.73 m^2 (SD 21.7) in both groups, and the mean baseline UACR was 284.3 mg/g (SD 3.6) and 288.9 mg/g (SD 3.5) in the finerenone and placebo groups, respectively, and approximately 88% of patients in FIDELIO and 50.7% of patients in FIGARO had very high albuminuria.
- CDEC discussed that maintaining and improving quality of life was identified as an outcome important to patients. However, the interpretation of HRQoL results is limited by the declining number of patients who completed these assessments over time and the lack of evidence of validity or minimal important difference for the Kidney Disease Quality of Life (KDQOL) and EuroQol Group 5-dimension, 5-level (EQ-5D-5L) questionnaires in patients with CKD and T2D; therefore, the impact of finerenone on HRQoL is unknown.
- CDEC noted that that the budget impact results presented for finerenone were analysed under the assumption it would also be used in patients currently receiving an SGLT2i. However, CDEC noted if finerenone were only used in individuals who

met the proposed initiation criteria, which excludes those currently receiving an SGLT2i, the budget impact would be substantially lower.

Background

Diabetes is the most common cause of kidney disease in Canada, and it is estimated by the sponsor that there are over 1 million people in Canada living with chronic kidney disease (CKD) and Type 2 Diabetes (T2D) in 2022. Older age, low socioeconomic status, obesity, smoking, poor glycemic and blood pressure control, and genetic factors are known risk factors for diabetic kidney disease. CKD is the leading cause of kidney failure [previously termed as end-stage renal disease (ESRD)] necessitating dialysis or renal transplant, CKD is also associated with cardiovascular (CV) complications leading to decreased quality of life and premature death. In a US survey that evaluated 15,000 patients with diabetes and kidney disease, 10-year mortality was 4-fold and 2.7-fold higher, and CV mortality was 3-fold and 6-fold higher in patients with both CKD and T2D compared to patients with either CKD or T2D alone, respectively. Patients with both CKD and T2D also reported lower HRQoL scores compared to those with CKD alone or T2D alone. CKD is clinically diagnosed in diabetic patients based on the presence of albuminuria (>30 mg/g) and/or decreased estimated glomerular filtration rate (eGFR <60mL/min/1.73m^2) in at least 2 out of 3 samples in a 3-month period. These are also 2 important indicators of disease progression: high urinary albumin-creatinine ratio (UACR) and low eGFR values indicate more severe disease.

According to the clinical experts consulted by CADTH, the primary goal of treatment is to reduce the risk of progression of CKD to ESKD by the application of pharmacologic and lifestyle strategies. The general approach to the management of patients with CKD and T2D includes optimization of blood pressure, proteinuria, and glycemic control, dietary changes, and lowering lipid levels with statins. In addition, for several decades, CKD patients have been treated with either an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) that inhibits the renin-angiotensin-aldosterone system (RAAS). Recently, guidelines have been revised to encourage the use of sodium-glucose co-transporter 2 (SGLT2) inhibitors in CKD patients with T2D, specifically for patients with severely increased albuminuria (>300 mg/g). Some patients may be intolerant to SGLT2 inhibitors, including patients with poor glycemic control, patients at high risk of genital infections or lower limb amputation, and patients with acute kidney injury. According to the clinical experts consulted by CADTH, there is limited access to SGLT2 inhibitors in Canada and access varies by jurisdictions, although access and subsequent use is expected to increase with time. In this review, the sponsor identifies SGLT2 inhibitors, in addition to ACE-inhibitors or ARBs as standard of care. Despite the application of the pharmacologic and lifestyle strategies, the clinical experts indicated that there is still a number of patients with both CKD and T2D who continue to progress to kidney failure or develop CV events, and that patients with CKD and T2D could benefit from additional pharmacologic therapies.

Finerenone has been approved by Health Canada as an adjunct to standard of care therapy to reduce the risk of end-stage kidney disease and a sustained decrease in estimated glomerular filtration rate, and cardiovascular death, non-fatal myocardial infarction and hospitalization for heart failure. Finerenone is a nonsteroidal, selective mineralocorticoid receptor antagonist (MRA). It is available as oral tablets and the recommended starting dose of finerenone is 20 mg once daily for patients with eGFR ≥60 mL/min/1.73 m^2 or 10 mg once daily for patients with eGFR ≥25 to <60 mL/min/1.73 m^2. Four weeks after initiation or re-start or up-titration of finerenone treatment, serum potassium and eGFR should be remeasured to determine continuation of finerenone treatment and dose adjustment. Thereafter, serum potassium should be remeasured periodically and as needed based on patient characteristics and serum potassium levels. Initiation of finerenone treatment is not recommended in patients with eGFR < 25 mL/min/1.73m^2 or in patients with serum potassium > 5.0 mmol/L. Treatment should be discontinued in patients with end-stage renal disease (eGFR < 15 mL/min/1.73m^2).

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- A review of the 2 Phase III, randomized, double-blind, placebo-controlled, clinical studies in patients with chronic kidney disease and type 2 diabetes.
- Patients perspectives gathered by patient groups, The Kidney Foundation of Canada and Diabetes Canada.
- Input from public drug plans that participate in the CADTH review process.

- Two clinical specialists with expertise diagnosing and treating patients with chronic kidney disease and cardiovascular disease.
- Input from one clinician group, LMC Diabetes and Endocrinology.
- A review of the pharmacoeconomic model and report submitted by the sponsor

Stakeholder Perspectives

Patient Input

Patient input for the review of finerenone was provided as a joint submission from The Kidney Foundation of Canada and Diabetes Canada. They conducted an online survey of patients with CKD and type 2 diabetes and their caregivers residing across Canada in May 2022 (n = 24; 9 completed and 15 partially completed the survey). A total of 8 respondents identified as patients with CKD, 1 respondent identified as a caregiver of a patient with CKD, and 6 respondents identified as patients with type 2 diabetes.

Survey respondents who identified themselves as living with both CKD and diabetes reported challenges with fatigue and anemia as well as adhering to dietary restrictions due to their high costs and inconvenience when dinning with others. Patients with CKD may often present with comorbidities; 7 respondents reported high blood pressure, 3 reported high cholesterol, 1 reported high potassium levels, 1 reported heart disease, and 1 reported having had a heart attack. One survey respondent stated feeling tired and unable to focus on certain tasks due to living with multiple medical conditions. Five respondents reported worsening of their CKD and 6 respondents indicated they have taken a medication to reduce the risk of worsening kidney disease, of which 3 reported experiences with ACE inhibitors and 2 reported experience with ARBs. Respondents also indicated experience with diuretics, tacrolimus, erythropoietin, and dapagliflozin [SGLT2 inhibitor]. Of the 6 survey respondents who indicated their level of satisfaction with their current medication(s), 3 were satisfied, 1 was very satisfied, and 2 were neutral.

Survey respondents identified the following factors as the most important considerations for new treatment options in CKD: 1) “does it make me feel tired;” 2) “does it interfere with my other medications;” and 3) “how much does it cost.” Survey respondents identified the following outcomes as important for new treatment options for both CKD with or without diabetes: 1) “limiting or arresting the progression of both diseases;” 2) “make kidneys better;” 3) “a longer life span;” and 4) “maintain and improve quality of life overall.”

Finally, the Kidney Foundation of Canada and Diabetes Canada indicated that patients living with CKD may experience significant financial challenges due to reduced income (e.g., missed time from work as a result of their symptoms) and increased expenses (e.g., high costs associated with treatment, frequent visits to the healthcare team, and hospitalization). According to the organizations, equitable access to medications that slow the progression of kidney disease and reduce the risk of cardiac events, such as finerenone, may help to relieve the financial burden of CKD and type 2 diabetes on patients and the healthcare system.

Clinician input

Input from clinical experts consulted by CADTH

The clinical experts mentioned that despite available therapies for patients with CKD and T2D, there is a need for additional treatment options that reduce the risk of progression to kidney failure or cardiovascular events. There are still patients who continue to progress to these outcomes and that can benefit from additional therapies such as finerenone. The clinical experts noted that the current paradigm aims to reduce progression of CKD to ESKD (kidney failure requiring dialysis or renal transplant). Treatment measures include blood pressure control, RAAS inhibition (ACE inhibitors and/or ARBs), and the use of SGLT2inhibitors, in addition to lifestyle changes, the use of statins and glycemic control. The clinical expert noted that finerenone may be combined with SGLT2 inhibitors to reduce cardiorenal risk as they protect kidney function through distinct and complementary pathways.

According to the clinical experts, finerenone should be considered for patients who remain with a significant residual proteinuria despite being on a maximal tolerated dose of ACEi/ARB and SGLT2i and noted that finerenone can be added to these therapies 3 months after initiating SGLT2i based on clinical experience. They also mentioned that patients who are unable to tolerate SGLT2i (e.g., due to hypotension or acute kidney injury) should be considered for finerenone. In the opinion of the clinical experts, treatment response can be assessed using surrogate measures such as changes in proteinuria over time, and stability of renal function

(eGFR). Intervals for monitoring should follow the current guideline recommendations [twice annually according to the American Diabetes Association].

According to the clinical experts, finerenone is better initiated as an add-on therapy in a specialist setting or in community setting but with specialist guidance and support. The clinical experts note that finerenone should be discontinued if the patient is unable to tolerate the drug because of AEs such as hyperkalemia not amenable to management (e.g., dietary changes and/or diuretics use) or hypotension.

Clinician group input

The views of the clinician groups were consistent with the views of the clinical experts consulted by CADTH. Clinician group input for the review of finerenone was provided as a submission prepared by clinicians representing LMC Diabetes and Endocrinology, a single-specialty group endocrinology practice with 13 clinics across 3 provinces (Ontario, Quebec, and Alberta).

The clinician group recognized that there is an unmet need for a medication that will address the significant decline in kidney function and cardiovascular disease in patients with type 2 diabetes despite the availability of RAAS blockers and SGLT2 inhibitors and in patients who experience intolerance to and side effects with the currently available treatment options. The clinician group indicated finerenone would be used as an add-on therapy to RAAS blockers with or without SGLT2 inhibitors in patients with type 2 diabetes and an ongoing risk for kidney disease progression and cardiovascular disease. Alternatively, finerenone would be used as the first add-on therapy in patients who were unable to tolerate or developed side effects with RAAS blockers or SGLT2 inhibitors.

With respect to the patient population that will most likely benefit from finerenone, the clinician group identified patients with an eGFR ≥ 25 ml/min/1.73m^2 and albumin to creatinine ratio (ACR) ≥ 34 mg/mmol or with an eGFR 25 to 90 ml/min/1.73^2 and ACR 3.4 to 33.9 mg/mmol. The patient population that was identified to be the least suitable for treatment with finerenone would be patients with a history of clinically significant hyperkalemia. Outcomes used in clinical practice would be preservation of eGFR over time, reduction in urine albumin to creatinine ratio (uACR), improved symptoms of heart failure or prevention of heart failure and reduced ER visits/hospitalizations.

Drug Program Input

Input was obtained from the drug programs that participate in the CADTH reimbursement review process. The following were identified as key factors that could potentially impact the implementation of a CADTH recommendation for finerenone:

- Relevant comparators
- Considerations for initiation of therapy
- Considerations for discontinuation of therapy
- considerations for prescribing of therapy
- system and economic issues

The clinical experts consulted by CADTH provided advice on the potential implementation issues raised by the drug programs.

Table 2. Responses to Questions from the Drug Programs

Implementation issues	Response
Relevant comparators	
Was placebo plus SOC a reasonable comparator to use in these studies? Could there have been an alternative?	CDEC agreed with the clinical experts consulted by CADTH that placebo plus SOC is a reasonable comparator.
The sponsor is asking for reimbursement of the drug as adjunctive SOC for patients with CKD and T2D. Does CDEC agree with the SOC defined by sponsor for the current landscape of therapy for CKD-T2D?	CDEC agreed with the clinical experts consulted by CADTH that SOC as defined by the sponsor is appropriate, however due limited data to support combination finerenone and SGLT2i therapy, CDEC recommended not to reimburse finerenone in patients receiving SGLT2i.

Implementation issues	Response
The sponsor indicated that standard of care therapies includes: • an ACEi or ARB, and • a SGLT2i, unless contraindicated or not tolerated	
The benefit status of SGLT2i varies across the country and in some is based on indication such as T2D and HF. Patients in jurisdictions that have SGLT2i as restricted would have to meet specific criteria before adding on finerenone. Would the need for this drug in patients with CKD and T2D have an effect on the current benefit status of SGLT2i?	The clinical experts consulted by CADTH indicated that the need for finerenone should not directly impact access to SGLT2i. CDEC disagreed with the clinical experts and noted that there is limited evidence for the combination of finerenone and SGLT2i therefore if finerenone is restricted to patients not receiving SGLT2i, this may impact access. For example, patients on finerenone who become eligible for SGLT2i therapy later would not have coverage for both.
The sponsor is asking for reimbursement of finerenone to use as adjunctive care of therapy to reduce hospitalizations in HF? Could there be an indication creep and need to use this medication just in patients with HF?	The clinical experts noted that in cardiology, MRA drugs are a fundamental part of guideline-based therapy, and a newer-generation agent with relative advantages over spironolactone and eplerenone would be welcomed, irrespective of whether the patient had CKD, T2D or both. This would not be viewed as an “indication creep” so much as an indication. CDEC disagreed with the clinical experts and noted that finerenone is only indicated for adult patients with both CKD and T2D, and any use for patients who do not have both CKD and T2D is off-label, and that finerenone is appropriate therapy for patients with HF only when it has a Health Canada indication. In addition, FIGARO and FIDELIO excluded patients with a clinical diagnosis of chronic heart failure with reduced ejection fraction and persistent symptoms (NYHA class II – IV) at the run-in visit.
Would there be a need for finerenone in patients with either CKD or T2D alone? If so, how would jurisdictions be expected to handle these requests?	The clinical experts noted that there would be a need for finerenone for patients with CKD or T2D alone only in situations where ACEi/ARBs and/or SGLT2i are not tolerated or, in rare instances, contraindicated. The prescribers can state these reasons to justify access to the medication as needed. This will rarely happens based on current clinical practice experience as there is no data to inform this question. The sponsor also noted that that there are no data to inform whether finerenone can be used in patients with either CKD or T2D alone; and so, treatment in this manner is expected to be rare in current clinical practice, and that that the anticipated Health Canada indication is for patients with both CKD and T2D; therefore, use in CKD alone would be off label. A clinical trial planned specifically to evaluate finerenone in the non-diabetic CKD patient population, is expected to be completed in 2025. CDEC noted that finerenone is only indicated for adult patients with both CKD and T2D, and that finerenone should not reimbursed for patients with CKD or T2D alone.
The sponsor acknowledges that since the conclusion of both trials, Canadian treatment practices have evolved for CKD-T2D; SGLT2i have received regulatory approvals and	CDEC agreed with the clinical experts that the beneficial effects of SGLT2i on renal outcomes in people with T2D are largely seen as a “class effect” at this point. Data is limited in this regard in people without diabetes to be conclusive.

Implementation issues	Response
contemporary guidelines recommend their use to reduce cardiorenal risk in CKD-T2D. • Forxiga is currently the only SGLT2i currently indication for patients with CKD in diabetic and non-diabetic patients. • There is an ongoing study for the indication to be reviewed by CADTH where the intervention is combination of finerenone and empagliflozin. • Would there be a preference for the requirement of one SGT2i over another when adding on finerenone? Would any SGLT2i be reasonable as defined by SOC	
Can the committee define intolerance or contraindication to a SGLT2i?	CDEC agreed with the clinical experts that intolerance or contraindication to a SGLT2i is defined as patients with persistent hypoglycemia or hypotension, acute kidney injury, and high risk of amputation.
Considerations for initiation of therapy	
What would CDEC's definition of CKD be for patients to meet initiation criteria? Are there specific lab markers or other parameters that would be required from patients?	The clinical experts indicated that definition of CKD for patients to meet initiation criteria is if they have CKD and persistent residual risk (albuminuria) despite an optimal use of ACEi or ARB and SGLT2i. The use of finerenone will be an add on therapy to modify risk in CKD in patients already optimized on the standard of care (ACE or ARB plus SGLT2i) and having serum potassium in the normal range (<5mmol/L) CDEC noted that KDIGO guidelines define CKD as "*persistently elevated urine albumin excretion (≥ 30 mg/g [3 mg/mmol] creatinine), persistently reduced estimated glomerular filtration rate (eGFR <60 ml/min per 1.73 m^2), or both, for greater than 3 months."*
Considerations for discontinuation of therapy	
What would CDEC define as disease progression for CKD and when would the medication be discontinued?	CDEC agreed with the clinical experts that the key factor that may drive discontinuation will be hyperkalemia. This will usually be on a temporary basis to control the hyperkalemia with dietary measures, reassess and reinitiate therapy. A permanent discontinuation is only warranted in case of hyperkalemia that is persistent and not amenable to dietary and/or therapeutic measures as is done with ACEi or ARBs. CDEC also noted that patients who progress to ESKD requiring dialysis or transplant should discontinue finerenone.
If the patient had a clinically significant CV event or hospitalization due to HF while on finerenone would treatment be discontinued?	CDEC agreed with the clinical experts that if the patient had a clinically significant CV event or hospitalization due to HF while on finerenone, treatment with finerenone should not be discontinued as finerenone would be used in lieu of one of the older MRAs. HF patients have readmissions for HF or admissions for other cardiac conditions (e.g., arrhythmia) while on an MRA and these drugs are not stopped just on account of that. In the specific example of arrhythmia, if this was VT/VF felt due to hyperkalemia that was due in turn to the MRA, then dosing might be adjusted; but it would not mean that the drug would automatically be stopped.
Considerations for prescribing of therapy	
Would this medication only be prescribed by a specialist, or would a general practitioner be able to initiate therapy?	CDEC agreed with the clinical experts that general practitioners will be prescribing the medication since they see the most

Implementation issues	Response
If only a specialist, which would be the most appropriate? (Cardiologist, nephrologist, or endocrinologist)	patients meeting the eligibility criteria for the drug (i.e., CKD with albuminuria and T2D).
System and economic issues	
• The submitted price per smallest dispensable unit of KERENDIA is $3.3400 per 10 mg or 20 mg tablet, which corresponds to a total cost of $3.3400 per day (once daily dosing) • Listing this drug as requested is estimated to result in incremental costs to the pan-Canadian public drug programs (excluding Québec) of $11,355,594 in Year 1, $33,056,871 in Year 2, and $54,075,690 in Year 3 With generic SGLT2i coming out soon would this have any impact on the substantial estimated incremental costs to the drug programs provided by the sponsor?	CDEC noted that if patients are restricted to receiving an SGLT2i or finerenone, the use of generic SGLT2i could decrease the overall budget impact.

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CDEC = Canadian Drug Expert Committee; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HF = Heart failure; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association; SGLT2is = sodium-glucose co-transporter-2 inhibitors; SOC = standard of care; T2D = Type 2 Diabetes; VT = ventricular tachycardia; VF = ventricular fibrillation.

Clinical Evidence

Pivotal Studies and Protocol Selected Studies

Description of studies

FIDELIO (N=5734) and FIGARO (N=7437) are 2 Phase III, randomized, double-blind, placebo-controlled, parallel-group, multicenter, event-driven studies of finerenone compared with placebo in patients with chronic kidney disease and type 2 diabetes. The 2 studies differed in their primary objective: the primary objective in FIDELIO was time to the first occurrence of a renal composite endpoint in both finerenone and placebo groups, while the primary objective of FIGARO was time to the first occurrence of the CV composite endpoint in both finerenone and placebo groups. Secondary objectives in each study included the primary objective of the other study, as well as time to first occurrence of a more severe renal composite endpoint, time to all-cause mortality, time to all-cause hospitalization, and change in UACR from baseline to Month 4. The studies were sponsored by Bayer and included 30 (FIDELIO) and 31 (FIGARO) study centers in Canada.

After a run-in period of up to 16 weeks and a screening period up to 2 weeks, eligible patients were randomized in a 1:1 ratio to the finerenone (10 mg or 20 mg) or placebo treatment arm, and stratified by region, eGFR category at screening, and albuminuria interval at screening. Randomization occurred at Visit 1 and then there were 3 more planned monthly visits, followed by a visit every 4 months until the end of the study. Finerenone drug dose could be up-titrated or down-titrated at any point following start of treatment at Visit 1. If patients stopped the study drug prematurely, they remained in the trial and were followed-up until the end of the study.

Patient demographic characteristics and key disease characteristics were balanced between the finerenone and placebo groups in both trials. The mean age in both groups in both studies was approximately 65 years old. Most patients in both trials were male ([69.8%]) and White [68.1%]). Mean baseline BMI across all groups was 31.3 (SD 6.0), 47.5% of patients had never smoked, and 59.8% were alcohol abstinent. In the FIDELIO trial, mean baseline eGFR was approximately 44 mL/min/1.73 m^2 (SD 12.5) in both groups, and mean baseline UACR was 798.8 mg/g (SD 2.7) and 814.7 mg/g (SD 2.7) in the finerenone and placebo groups respectively. In FIGARO, mean baseline eGFR was approximately 68 mL/min/1.73 m^2 (SD 21.7) in both groups, and mean baseline UACR was 284.3 mg/g (SD 3.6) and 288.9 mg/g (SD 3.5) in the finerenone and placebo groups, respectively. Regarding medication use at baseline, 66% of patients in FIDELIO and 57% of patients in FIGARO were on ARBs, and 34% of patients in FIDELIO and 43% of patients in FIGARO were on ACEis. Across the 2 trials, 97.7% of patients were also on anti-diabetic treatment, including 6.7% of patients who were on SGLT2 inhibitors.

Efficacy Results

In FIDELIO, the primary and key secondary endpoints met the pre-planned criteria for significance and all-cause mortality, the next secondary endpoint, was tested hierarchically and it did not reach statistical significance and so the remaining secondary endpoints were tested in an exploratory manner. In FIGARO, the primary endpoint met the pre-planned criteria for significance, and the key secondary endpoint did not, therefore the remaining secondary endpoints were tested in an exploratory manner.

The primary outcome in the FIDELIO study was time to first occurrence of the 40% renal composite endpoint which is comprised of onset of kidney failure, a sustained decrease of eGFR ≥40% from baseline over at least 4 weeks, or renal death, hereafter referred to as the 40% renal composite endpoint. The 40% renal composite endpoint was a key secondary endpoint in FIGARO. In FIDELIO, this composite outcome occurred in 504 (17.8%) and 600 (21.1%) of patients in the finerenone and placebo groups respectively, and the HR was 0.825 (95% CI 0.73 to 0.93, p-value =0.0014) in favor of finerenone. In FIGARO, this endpoint occurred in 350 (9.5%) and 395 (10.8%) patients in the finerenone and placebo groups respectively, and the HR was 0.87 (95% CI 0.76 to 1.01, p-value =0.0689) which was not statistically significant. In the pooled analysis of FIDELIO and FIGARO, the HR was 0.85 (95% CI 0.77 to 0.93) and 0.77 (95% CI 0.67 to 0.88) for the 40% and 57% renal composite endpoints respectively, in favour of finerenone.

The 57% renal composite endpoint was a secondary endpoint in both studies. In FIDELIO it occurred in 252 (8.9%) and 326 (11.5%) patients in the finerenone and placebo groups respectively, and the HR was 0.76 (95% CI 0.65 to 0.90) in favor of finerenone. In FIGARO it occurred in 108 (2.9%) and 139 (3.8%) patients in the finerenone and placebo groups respectively, and the HR was 0.77 (95% CI 0.60 to 0.99) in favor of finerenone. In FIDELIO, the individual components of sustained decrease in eGFR ≥40% and eGFR ≥57% (relative to baseline) had HRs of 0.815 (95% CI: 0.722 to 0.920) and 0.68 (95% CI: 0.55 to 0.82) respectively, and were the main drivers of the composite outcome results. The treatment effect of finerenone was assessed across the following subgroups of patients: history of CV disease, eGFR category at baseline, type of albuminuria at baseline, and SGLT2 inhibitors treatment at baseline. In general, the treatment effect of finerenone on the primary endpoint (time to first occurrence of the 40% renal composite endpoint) was consistent with the primary analysis across patient subgroups with the following exception: In FIDELIO, HR was greater than 1 in patients who were treated with SGLT2 inhibitors at baseline, favoring placebo over finerenone, yet the small sample size and wide CIs in this subgroup reflects uncertainty in the effect estimates. In FIGARO, HR was also greater than 1 in patients with eGFR 45 to < 60 mL/min/1.73 m^2 at baseline, and in patients with high albuminuria (30 to < 300 mg/g) at baseline.

Baseline values of UACR were comparable between the treatment groups but differed between trials according to the inclusion criteria, with higher values in the FIDELIO trial population. Nevertheless, in both trials, the change in UACR from baseline to Month 4 was larger in the finerenone group than in the placebo group, with a ratio of least-squares (LS) mean change from baseline (95% CI) of 0.69 (0.66 to 0.72) and 0.68 (0.65 to 0.70) in FIDELIO and FIGARO respectively, with p-value <0.0001.

Baseline values of eGFR were comparable between the treatment groups but differed between trials according to the inclusion criteria, with lower values in the FIDELIO trial population. There was a larger acute reduction in eGFR in the finerenone group than in the placebo group with an LS-mean difference between groups at Month 4 of -2.38 (95% CI -2.77 to -1.98) and -2.24 (95% CI -2.67 to -1.80) in FIDELIO and FIGARO respectively, with a p-value of <0.0001. The decrease in eGFR in the finerenone group then slows down, until the difference between both groups becomes positive, indicating a slower rate in eGFR decline rate in the finerenone group than in the placebo group at Month 28 in the FIDELIO trial and Month 36 in the FIGARO trial.

The primary outcome in the FIGARO study was time to first occurrence of the cardiac composite endpoint which is comprised of CV death, non-fatal MI, non-fatal stroke, or hospitalization for heart failure. The CV composite endpoint was a key secondary endpoint in FIDELIO. In FIDELIO, this composite outcome occurred in 367 (13%) and 420 (14.8%) of patients in the finerenone and placebo groups respectively, and the HR was 0.86 (95% CI 0.75 to 0.99, p-value = 0.0339) in favor of finerenone. In FIGARO, this endpoint occurred in 458 (12.4%) and 519 (14.2%) patients in the finerenone and placebo groups respectively, and the HR was 0.87 (95% CI 0.76 to 0.98, p-value = 0.0264) in favor of finerenone. In the pooled analysis of both trials, the HR was 0.86 (95% CI 0.78 to 0.95) with p-value = 0.0018, in favor of finerenone. In FIGARO, the only individual component of statistical significance was hospitalization due to heart failure had a HR of 0.71 (95% CI: 0.56 to 0.90) in favour of finerenone. In both trials, there was almost no difference in risk of non-fatal stroke with HR of 0.97 (95% CI: 0.74 to 1.26) in FIDELIO and of 1.03 (95% CI: 0.77 to 1.38) in FIGARO. The treatment effect of finerenone on the time to first occurrence of the cardiac composite endpoint was assessed across the following subgroups of patients: history of CV disease, eGFR category at baseline, type of albuminuria at baseline, and SGLT2 inhibitors

treatment at baseline. In general. the treatment effect of finerenone was consistent with the primary analysis across patient subgroups with the following exception: HR was approximately 1 in patients who were treated with SGLT2 inhibitors at baseline in FIDELIO, while HR was 0.49 (95% CI 0.28 to 0.86) in FIGARO. However, the small sample size of this patient group in both trials reflects uncertainty in the effect estimates.

Incidence of all-cause mortality was similar between both groups in both trials, with 552 (8.5%) and 614 (9.4%) deaths from any cause in the finerenone and placebo groups, respectively. Comparing the finerenone group with the placebo group, the HR was 0.90 (95% CI 0.75 to 1.07) in FIDELIO and 0.89 (95% CI 0.77 to 1.04) in FIGARO.

Incidence of all-cause hospitalization was similar between both groups in both trials, with 2836 (43.5%) and 2926 (45.0%) patients hospitalized for any cause in the finerenone and placebo groups, respectively. More hospitalizations were non-CV related (35%) than CV-related (19%). Comparing the finerenone group with the placebo group, the HR was 0.95 (95% CI 0.88 to 1.02) in FIDELIO and 0.97 (95% CI 0.90 to 1.04) in FIGARO.

At baseline, mean KDQOL_36 summary scores in all domains were comparable between treatment groups in each trial, and between both trials, except for the “burden of kidney disease” domain where patients in the FIGARO group scored relatively higher than in FIDELIO. The quality of life decreased over time all patients, consistently in all domains, assessed until Month 36 in FIDELIO and Month 48 in FIGARO. The physical component summary showed a sustained difference in favor of finerenone in FIDELIO at Month 12 (LS mean difference = [redacted] and Month 24 (LS mean difference = [redacted], and in FIGARO at Month 36 (LS mean difference = [redacted].

Harms Results

A total of 5602 (86.1%) patients in the finerenone group and 5607 (86.4%) patients in the placebo group experienced at least one adverse event (AE). The most common AE in the finerenone group was hyperkalemia (14% vs 6.9% in the placebo group) and the most common AEs in the placebo group were hypertension (9% vs 6.4% in the finerenone group) and peripheral oedema (5.9% vs 9% in the finerenone group). A total of 2060 (31.6%) patients in the finerenone group and 2186 (33.7%) in the placebo group experienced at least one serious adverse event (SAE). The most commonly reported SAE was pneumonia (2.2% in the finerenone group vs 3.3% in the placebo group).

A total of 414 (6.4%) patients in the finerenone group and 351 (5.4%) in the placebo group stopped treatment due to adverse events. There was a total of 110 (1.7%) and 151 (2.3%) deaths due to TEAEs in the finerenone and placebo groups, respectively.

In terms of notable harms, more patients reported hypotension in the finerenone group than in the placebo group (4.6% vs 3.9%). The number of patients who experienced atrial flutter and atrial fibrillation was less than 1% in each treatment group and comparable between groups. The number of patients who experienced hospitalization due to hyperkalemia was higher in the finerenone group compared to the placebo group (0.9% vs 0.2%).

Critical Appraisal

Key baseline demographic and disease characteristics and past history of medication used appear to be balanced between the finerenone and placebo groups in both trials. There were important protocol deviations, balanced between treatment groups, reported in 53% and 58.5% of patients in FIDELIO and FIGARO, respectively. Due to study timelines, more protocol deviations associated with the COVID-19 were reported in FIGARO than FIDELIO, however deviations were balanced between treatment groups, and supportive analyses did not uncover any notable effect of the COVID-19 pandemic on the treatment effect of finerenone. The interpretation of results for the HRQoL instruments (i.e., the ability to assess trends over time and to make comparisons across treatment groups) is limited by the significant decline in patients available to provide assessment over time as well as lack of evidence of validity or MID of the HRQoL questionnaires used in the trials in patients with CKD and T2D. In the prespecified FIDELITY pooled analysis combining both trials, patients in FIDELIO had a lower eGFR at baseline than FIGARO, and the mean treatment duration was longer in FIGARO (approximately 35 months) than in FIDELIO (approximately 27 months). The statistical analysis in FIDELITY was exploratory and descriptive in nature with no adjustment for multiplicity, however, pooling is considered appropriate.

According to the clinical experts consulted by CADTH for this review, the demographic and disease characteristics of both study populations were generally reflective of the Canadian population with CKD and T2D. They agreed that there was an overrepresentation of male patients (70% to 30%), whereas they noted there should be a more proportionate representation of patients, given potential differences in treatment efficacy and safety. The product monograph indicates that patients with eGFR ≤25 ml/min/1.73 m^2 should not start finerenone, however 2.4% of patients in FIDELIO reported a baseline eGFR ≤25 ml/min/1.73 m^2 (potentially due to decline in eGFR between screening and randomization). While the trials were underway, the SOC for patients with CKD and T2D evolved to include SGLT2i. Therefore, only 6.7% of patients in both trials (n=877) were on a SGLT2i at baseline, and patients were not stratified by SGLT2i use, however use at baseline was balanced between the 2 treatment groups in both trials. In addition, the proportion of patients using GLP-1 agonists with and without SGLT2i at baseline was not balanced (18.5% vs 6.4%). This may have confounded the subgroup findings as GLP-1 agonists may also improve cardiorenal outcomes in patients with CKD and T2D. The clinical experts consulted by CADTH agreed that placebo plus SOC was an appropriate comparator in Canadian clinical practice for patients with CKD and T2D. The clinical experts agreed with the sponsor's definition of SOC would include ACEi or ARBs, and ideally SGLT2i, which is still not widely accessible to Canadian patients with CKD and T2D. The clinical experts pointed out that a combination therapy with the 2 agents together makes physiological sense as SGLT2i are linked to reductions in the risk of hyperkalemic episodes (serum potassium ≥6.0 mmol/L), and finerenone has hyperkalemia as a side effect. There is, however, limited evidence on the positioning of finerenone with regards to SGLT2i, and the evidence available for the addition of finerenone to ACEi or ARB, and a SGLT2i is limited. A non-sponsor submitted reimbursement review assessing the use of SGLT2i in patients with CKD and T2D is currently ongoing. A phase 2 RCT that will compare finerenone plus placebo, SGLT2inhibitors plus placebo, and finerenone plus SGLT2 inhibitors (CONFIDENCE trial) will initiate in 2022, and results may provide more insight into this comparison and the place in therapy of finerenone. Finally, the trials included composite renal and CV outcomes and were only powered for their respective primary composite outcomes and not to the components of the primary outcome which include sustained decrease in eGFR and initiation of ESKD in FIDELIO, and hospitalization due to heart failure in FIGARO, hence the impact of finerenone on each of the components of the composite outcomes is uncertain.

Indirect Comparisons

Indirect evidence from 1 published network meta-analysis (NMA) by Zhao et al. (2022) evaluated the effectiveness of finerenone compared to SGLT2 inhibitors in the treatment of CKD and T2D. SGLT2 inhibitors are currently part of the standard of care for patients with diabetic kidney disease, however, only 6.7% (877 out of 13,026) patients in the pivotal trials were concurrently taking SGLT2 inhibitors in the FIDELIO and FIGARO trials. This NMA, therefore, provide an indirect comparison of efficacy outcomes between finerenone and SGLT2 inhibitors.

Description of studies

The authors include 14 articles reporting 8 placebo-controlled RCTs comprising 30,661 patients. Seven studies involved an assessment of SGLT2 inhibitor (13,246 patients receiving gliflozin vs 11,741 receiving placebo): EMPA-REG OUTCOME, CANVAS Program, CREDENCE, DECLARE–TIMI 58, DAPA-CKD, VERTIS CV, and SCORED. One study (the pivotal FIDELIO trial) assessed finerenone (2,833 patients receiving finerenone vs 2,841 receiving placebo). According to Risk of Bias assessment, there was low risk of bias in all 8 studies.

MACE was defined consistently across the included studies. Kidney function progression (KFP), however, was defined differently across the included studies, with composite endpoints that included ESKD, renal death, and sustained decrease in eGFR that ranged from 40% to 50%. One trial included patients who had initiated renal replacement therapy (EMPA-REG OUTCOME), and 2 trials included patients with kidney transplants (DAPA-CKD and SCORED). One trial (VERTIS CV) did not report a renal composite endpoint. The authors considered these definitions similar enough to be used in the meta-analysis.

Efficacy Results

NMA results showed that, compared to finerenone, SGLT2 inhibitors significantly reduced the risks of KFP (HR 0.78, 95% CI 0.67 to 0.90) and hospitalization for heart failure (HHF) (HR 0.71, 95% CI 0.55 to 0.92). No treatment was favored when finerenone was compared to SGLT2 inhibitors for the outcomes of major adverse CV events (HR 0.95, 95% CI 0.71 to 1.27), nonfatal MI (HR 0.91, 95% CI 0.64 to 1.30), nonfatal stroke (HR 0.70, 95% CI 0.35–1.39), CV death (HR 1.00, 95% CI 0.78 to 1.29), and all-cause death

(HR 0.96, 95% CI 0.75 to 1.23). Network plots for all outcomes did not have any closed loop, suggesting a lack of direct evidence between finerenone and SGLT inhibitors, so an inconsistency test was not performed.

Harms Results

The safety outcomes of both treatments were not assessed in this NMA.

Critical Appraisal

This NMA included a limited number of studies with some heterogeneity in the definition a key renal outcome across the studies. Only 1 study assessed finerenone while the other 7 assessed an SGLT2i, which limited the statistical power of this NMA. The second pivotal RCT on finerenone from this review (FIGARO) was not included in this NMA and may have strengthened this analysis. The authors did not explore the baseline demographic characteristics of the patient populations across the trials and report that "the cardiorenal risk of participants was possibly different among included trials". The durations of the trial were not reported and may have differed between studies. Moreover, the safety outcomes of both treatments were not assessed in this NMA. The CADTH review team was unable to rigorously assess the methods in this article because insufficient details on the methods were provided (e.g., no details on the retrieved number of records in the systematic review), and there was no discussion on possible adjustments for potential effect modifiers or feasibility assessment. A small proportion of patients in the included FIDELIO trial were using SGLT2i at baseline, but no additional analysis including and excluding this subgroup was conducted.

Economic Evidence

Cost and Cost-Effectiveness

Component	Description
Type of economic evaluation	Cost-utility analysis Markov model
Target population	Health Canada indication: Adults with CKD and T2D Reimbursement request: Adults with CKD and T2D as an adjunct to SoC that consists of an ACEi or ARB, and a SGLT2i, unless contraindicated or not tolerated.
Treatment	Finerenone plus SoC
Dose regimen	Starting: • 20 mg once daily if eGFR ≥ 60 mL/min/1.73m^2 • 10 mg once daily if eGFR ≥ 25 to < 60 mL/min/1.73m^2 Target: • 20 mg once daily
Submitted price	Finerenone, 10 mg, tablet: $3.3400 Finerenone, 20 mg, tablet: $3.3400
Treatment cost	$1,219 annually
Comparator	SoC (consisting of an ACEi or ARB, and a SGLT2i, unless contraindicated or not tolerated) along with other concomitant medications for glucose management and/or cardiovascular complications (e.g., BB, diuretics, calcium antagonists, statins, platelet aggregation inhibitors, insulin, metformin, acarbose, sulfonylurea, DPP-4 inhibitors, GLP-1 agonists)
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, LYs
Time horizon	Lifetime (35.2 years)
Key data source	FIDELITY, a pre-specified pooled efficacy and safety analysis, combining data from FIDELIO-DKD and FIGARO-DKD (NCT02545049): two phase III, randomized, double-blind, placebo-controlled, multicentre clinical trials designed to investigate the effect of finerenone on reducing kidney failure and disease progression and on reducing CV mortality and morbidity, respectively.
Key limitations	• The sponsor's model structure may not adequately reflect the progressive nature of chronic kidney disease. The model allows for substantial improvements in kidney function resulting in reduced mortality risk and improved quality of life, contrary to what would be expected in this disease area. The model predicts that patients may have improved kidney function (measured through sustained improvements in eGFR score), to the extent an individual with an eGFR < 15

Component	Description
	ml/min per 1.73 m^2 may return to normal kidney function. This was considered highly unlikely by CADTH clinical experts. • The influence of SGLT2i as a component of standard of care is uncertain. If SGLT2is become standard of care for this indication, it is unclear what the additional benefit of finerenone will be. In the trials, only 6.7% of patients were on SGLT2is; therefore, there is not sufficient evidence to conclude what the relative and absolute risk reduction, regarding clinical parameters reviewed in the trial, would be for those also receiving finerenone. • The impact on dialysis reduction is uncertain. In the model patients on finerenone progress at a slower rate to CKD5, at which point dialysis is initiated – meaning patients on finerenone are less likely to receive dialysis. Further, patients who reach CKD5 while on finerenone were also assumed to have a lower risk of requiring dialysis – further reducing the rate of dialysis. It is unclear to what degree the clinical data supports the latter assumption. • The impact on mortality is uncertain as the trials showed no statistically significant mortality reduction in the finerenone arm relative to placebo. • In the model, the sponsor assumes a reduction in MIs and stroke for patients on finerenone, which was not seen in the trials. The sponsor assumed that the HR for any CV event from the trials would apply to all individual CV events, such that finerenone would reduce all CV events equally. This was not observed for the individual CV outcomes from the trial where statistically significant reductions in HF hospitalisations were seen but there were limited to no reductions in MIs and strokes. • Health state utility values derived from the trial were consistently higher than those seen in the literature for CKD especially given the population being analyzed also has T2D as a comorbidity. • Health state costs for CKD states exclude relevant health system costs. This overestimates the predicted cost savings generated from finerenone usage.
CADTH reanalysis results	• CADTH was unable to conduct a base case analysis as key limitations within the analysis could not be addressed given the structure of the model and available clinical information. CADTH notes these limitations likely favour finerenone and therefore the exploratory analyses performed by CADTH likely underestimate the true ICER. • Due to uncertainty regarding concurrent use of finerenone with SGLT2is, CADTH was unable to conduct a reliable reanalysis in the reimbursement request population; instead, all reanalyses are reflective of the proposed Health Canada indication population. • CADTH conducted five exploratory reanalyses: in exploratory reanalysis 1 CADTH used health state utility values from the literature, updated CKD state costs and aligned dialysis prevention in CKD 5 with that from the trial; in exploratory reanalysis 2 CADTH further removed MIs and strokes from the analysis; in reanalysis 3 CADTH further removed finerenone's benefit on CV death; in reanalysis 4 CADTH further assumed no reduction in dialysis for those who reach CKD 5; in exploratory reanalysis 5 CADTH further assumed both a lower rate of dialysis reduction and no CV death benefit from finerenone. ○ Reanalysis 1: ICER of $70,052 per QALY gained (inc. costs: $6,406; inc. QALYs: 0.09), 23% price reduction needed to achieve an ICER < $50,000 per QALY ○ Reanalysis 2: ICER of $73,484 per QALY gained (inc. costs: $6,935; inc. QALYs: 0.09), 29% price reduction needed to achieve an ICER < $50,000 per QALY ○ Reanalysis 3: ICER of $175,549 per QALY gained (inc. costs: $3,293; inc. QALYs: 0.02), 31% price reduction needed to achieve an ICER < $50,000 per QALY ○ Reanalysis 4: ICER of $93,752 per QALY gained (inc. costs: $7,333; inc. QALYs: 0.08), 44% price reduction needed to achieve an ICER < $50,000 per QALY ○ Reanalysis 5: ICER of $2,994,490 per QALY gained (inc. costs: $4,256; inc. QALYs: >0.01), 55% price reduction needed to achieve an ICER < $50,000 per QALY

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; HF = heart failure; HR = hazard ratio; ICER = incremental cost-effectiveness ratio; LY = life-year; MI = myocardial infarction; QALY= quality-adjusted life-year; SGLT2i = sodium-glucose cotransporter-2 inhibitor; T2D = type 2 diabetes.

Budget Impact

CADTH's reanalyses of the sponsor submitted budget impact assumed T2D CKD patients with concomitant chronic HF would be eligible for finerenone and included mark-ups and dispensing fees. CADTH reanalyses suggest that the overall budget impact to the public drug plans of reimbursing finerenone in the Health Canada indication, regardless of what constituted standard of care, is expected to be $148,282,507 over three years (Year 1: $17,075,144; Year 2: $49,750,884; Year 3: $81,456,478).

CDEC Information

Members of the Committee:

Dr. James Silvius (Chair), Dr. Sally Bean, Mr. Dan Dunsky, Mr. Morris Joseph, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Dr. Christine Leong, Dr. Kerry Mansell, Dr. Alicia McCallum, Dr. Srinivas Murthy, Ms. Heather Neville, Dr. Danyaal Raza, Dr. Emily Reynen, and Dr. Peter Zed.

Meeting date: October 27, 2022

Regrets:

One expert committee member did not attend.

Conflicts of interest:

None