Stakeholder Input

Disclaimer: The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. As such, they are independent of CADTH and do not necessarily represent or reflect the view of CADTH. No endorsement by CADTH is intended or should be inferred.

By filing with CADTH, the submitting organization or individual agrees to the full disclosure of the information. CADTH does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting organization or individual and all conflict of interest information are included in the submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

CADTH is committed to treating people with disabilities in a way that respects their dignity and independence, supports them in accessing material in a timely manner, and provides a robust feedback process to support continuous improvement. All materials prepared by CADTH are available in an accessible format. Where materials provided to CADTH by a submitting organization or individual are not available in an accessible format, CADTH will provide a summary document upon request. More details on CADTH's accessibility policies can be found *here*.

Patient Input

The Kidney Foundation of Canada

About the Kidney Foundation of Canada

Over nearly six decades, the Kidney Foundation of Canada has been guided by the fundamental principles of innovation, leadership, and collaboration, and has been committed to excellent kidney health, optimal quality of life for those affected by kidney disease, and a cure.

The Kidney Foundation of Canada is the leading charity committed to eliminating the burden of kidney disease through:

Funding and stimulating innovative research for better prevention, treatments and a cure;

Providing education and support to prevent kidney disease in those at risk and empower those with kidney disease to optimize their health status;

Advocating for improved access to high quality health care;

Increasing public awareness and commitment to advancing kidney health and organ donation.

For more information, please visit kidney.ca.

Information Gathering

Patient input was collected in July and August 2022 by the Kidney Foundation of Canada in both official languages via a self-administered questionnaire to people across Canada. The survey was directed at people living with chronic kidney disease and their caregivers and inquired about respondents' lived experience with chronic kidney disease and medications and expectations for new drug therapies in Canada. The survey also posed questions specifically about the drug under review, dapagliflozin. Awareness about the surveys was generated through the Kidney Foundation's social media channels (Twitter and Facebook), as well as the Kidney Foundation website.

A total of 36 people responded to the survey with 18 completed and 18 partially completed surveys. Of the 12 people who responded to the questions about their current age or the current age of the person they care for, 1 was between the age of 15 and 24, 2 were aged 25 to 39, 2 were between the ages of 40 and 54, 3 were 55 to 69 years old, and 3 were over 70 years old. One person preferred not to answer.

19 respondents identified as being a person living with chronic kidney disease and 2 identified as being a caregiver for a person with chronic kidney disease.

Disease Experience

Kidney disease describes a variety of diseases and disorders that affect the kidneys. Most diseases of the kidney attack the nephrons and damage their ability to eliminate wastes and excess fluids. High blood pressure is one of its leading causes, and kidney disease can often lead to additional medical conditions, including heart disease.

Chronic kidney disease (CKD) is the presence of kidney damage, or a decreased level of kidney function, for a period of three months or more. Kidney disease can range from mild to severe and in some cases, can lead to kidney failure (sometimes referred to as end-stage kidney disease, or ESKD). There are usually no specific symptoms of kidney disease until the damage is severe. When the kidneys fail, wastes accumulate in the body and dialysis treatments or a kidney transplant are needed to survive.

Dialysis is the most common treatment for kidney failure, with kidney transplant being another option. There are two types of dialysis: peritoneal dialysis and hemodialysis. Canadians with kidney failure and their families face significant out-of-pocket costs. This burden is further compounded by the loss of income that is often associated with starting dialysis. It is important to note that

poverty is a determinant of health. This means that patients and their families that live in poverty may not be able to achieve optimal management of their medical issues.

In the early stages of chronic kidney disease, self-management strategies such as engaging in regular physical activity, maintaining a healthy body weight, stopping smoking and reducing sodium, and managing other medical conditions and medications may slow or stop damage to the kidneys.

Most survey respondents reported that chronic kidney disease has had a significant effect on their quality of life. One person said "*CKD impacts every aspect of my life, physically, emotionally, financially. My quality of life is poor because of medication side effects.*"

38% of respondents indicated that they have had to give up or reduce their physical activity, including one person who said that they "*can barely exercise due to lower energy levels*."

29% of the people surveyed reported that they've had to stop working or reduce their hours, including a caregiver who said they "*had to take a leave of absence from work to help my loved one with day to day chores.*"

Many of the survey participants also indicated that time family and friends was affected. One person said they are "*[…] unable to do fun things with family and friends due to frequent hospitalizations and depression.*" The were many reports of fatigue: "[…] *my kids are very young and I want to play with them but whenever I try to play with them I got tired in 15 minutes*", and *"[…] my family has to adjust plans to make sure I have places to rest or can sit out with something to do*."

There was also frequent mention of insomnia, with one person saying that they are "unable to sleep without multiple medications" and another stating "sleep is very difficult to get most nights." Other symptoms reported included itchiness, swelling, dizziness and nausea/vomiting.

In addition, many people dealing with CKD have a number of other conditions. Over 71% of respondents reported having or having had high blood pressure and 48% reported high cholesterol.

Experiences With Currently Available Treatments

Of the 20 respondents to a question about whether they've ever taken medication to reduce the risk of worsening kidney disease, 45% said that they had, and 35% said that they had not. 20% did not know. 33% of respondents to a question about specific medications said that they take or have taken angiotensin-converting enzyme (ACE) inhibitors, 44% reported taking angiotensin-receptor blockers (ARBs), and 22% said that they are taking flozins/SGLT2 inhibitors. Other medications included atorvastatin, bisoprolol, and mycophenolate, and there was also mention of the use of calcium, iron, and vitamin D.

9 people responded to a question about how satisfied they are with their current medication/blend of medications, and of those 1 reported being satisfied, 2 very satisfied, and 4 neither satisfied nor unsatisfied. 2 were unsatisfied. When asked about the challenges or difficulties they've experienced with their existing treatments, one respondent said "*ease of access*," and another said that "*some medications are not covered under any drug private or OHIP*." Others respondents reported that remembering to take medications and the number of medications are issues.

Improved Outcomes

When asked about their expectations for CKD therapies, respondents rated these questions as most important: Does it interfere with my other medications? "Does it affect my mood? How much does it cost?" "How long will I be on it?" Survey participants mentioned that side effects were important, as are cost and availability.

Overwhelmingly, respondents' hopes for new therapies for CKD were increased energy and increased well-being and quality of life. Other important expectations included less medication overall, less time away from work, and fewer hospital visits.

Experience With Drug Under Review

21 people responded to a question about their experience with dapagliflozin. 17 indicated that they have never taken it, with 2 indicating that they have. Both paid out of pocket for the prescription. The remaining 2 respondents said they did not know whether they've taken dapagliflozin.

Both respondents who have had experience with dapagliflozin reported that their dizziness was about the same. Other effects listed as "much better" by both patients included potassium levels and sodium levels, while tiredness/weakness, high blood pressure, nausea/vomiting, trouble breathing, and swelling/edema were also considered better by one person. Tiredness/weakness, high blood pressure, and low blood pressure were deemed worse by one participant each.

Companion Diagnostic Test

Not applicable to this submission.

Anything Else?

Living with chronic kidney disease can involve not only health and quality of life challenges, but significant financial challenges as well. People may experience a decrease in income if they must limit their working hours due to their condition, and at the same time out-of-pocket costs increase as they change their diet, begin taking medications, and follow up more often with their health care team. Those living with kidney disease also tend to be part of a low income and high cost population, and government coverage and financial support varies across jurisdictions, which can lead to inequities. For more on the financial burden of kidney disease, visit https://kidney.ca/GetInvolved/Be-Their-Voice/Financial-Burden-of-Kidney-Disease.

Should chronic kidney disease progress to kidney failure, hemodialysis is the most common treatment. The cost of hemodialysis to the health care system per person per year ranges from $56,000 to $107,000, so the savings to the system associated with slowing the progression of kidney disease are significant. Hospitalization and treatment of cardiac events in patients with chronic kidney disease also represent a significant cost to the health care system.

The financial burden of kidney disease and the treatment of associated heart disease means that many would benefit from effective, affordable treatments that they can access equitably and in a timely manner. As dapagliflozin may slow the progression of kidney disease and reduce the risk of cardiac events, it should be available as an option for people living with CKD.

Patient Group Conflict of Interest Declaration – The Kidney Foundation of Canada

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   There was no external assistance in completing this submission.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   There was no external assistance with data collection or analysis for this submission.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Alexion Pharma Canada Corp		X		
Amgen Canada				X
Astra Zeneca Canada				X
Bayer		X		
GlaxoSmithKline Inc.			X	
Horizon Pharma Inc.				X
Janssen Pharmaceutical Companies				X
Otsuka Canada Pharmaceutical Inc.				X
Paladin			X	
Takeda	X			

Canadian Association of Retired Persons (CARP)

About Canadian Association of Retired Persons (CARP)

CARP—A New Vision of Aging is Canada's largest advocacy association for older Canadians promoting equitable access to health care, financial security, and freedom from ageism. Backed by more than 330,000 members, CARP is a non-partisan association that has been around for over 40 years, committed to working with all parties in government to advocate for older Canadians. Our mission is to advocate for better healthcare, financial security, and freedom from ageism. CARP members engage in polls and petitions, email their elected representatives. https://www.carp.ca/

Information Gathering

We decided to conduct a survey (attached) with the hopes of understanding how many people are affected by CKD and the drug that they are currently on. In our Survey we found that 9.4%(about 39 people) of all results were on a drug that ended in -Flozin. Our Demographic is 45 plus, our region which we conducted in Canada, the results were taken from August 15-19th 2022.

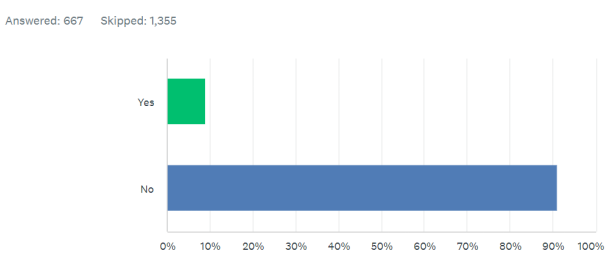
Here is our breakdown of just how many people are currently affected or worried about it.

Living with chronic kidney disease (CKD)	15.88%	321
A friend or family member with CKD	8.70%	176
Caring for someone living with CKD	1.98%	40
Concerned about kidney health	39.17%	792
None of the above	34.27%	693
TOTAL		2,022

DESCRIPTION OF IMAGE 5 questions in a table asking:
"Please select the answer that best describes you:"

Living with CKR	15.88% - 321 people
A friend or family member with CKD	8.70% - 176 people
Caring for someone living with CKD	1.98% - 40 people
Concerned about Kidney Health	39.17% - 792 people
None of the Above	34.27% - 693 people
Total	2022 people

Those who answered "None of the above" skipped the survey and got a questions asking if they were ever tested for CKD:



ANSWER CHOICES	RESPONSES	
Yes	9.00%	60
No	91.00%	607

DESCRIPTION OF IMAGE: bar graph with the question "Have you ever been tested for CKD?"

Yes 9% 60 people
No 91% 607 people

While 91% indicated they were not tested, it's worth noting that some may have had blood or urine work done by health professionals to assess kidney function without the patient being educated on this. Either way, this speaks to either a lack of testing or a lack of education about testing, both problematic"

Disease Experience

We had a number of people express concerns about no longer being able to travel or drastically change diets and lifestyles to maneuver around CKD. In response to the question “Could you please provide more details on how CKD impacts your day-to-day activities?” We had someone give us this: *Very tired - very low platelets and hemoglobin. Often suffer from chills.*
Issues with short term memory. Diet restrictions make meal planning a challenge. Drugs cause dizziness and constipation. Kidney issues also related to gout.”

The sentiments in the quote above are sadly seen repeated throughout the open form questions. Reading throughout it we hear the loud voices of people constantly being fatigued, frequent urination and low morale.
With someone even saying this: *“ I have the beginning of CKD as a diabetic at age 80. At this early stage, the disease is invisible.”*

Experiences With Currently Available Treatments

Our survey did not quantitatively address this question but our respondents provided qualitative information.
“More public information as to the damage certain pharmaceuticals create on kidneys and other body parts such as proton pump inhibitors and aspirins. All older patients getting getting new meds should have kidney function tests within 48 hours or so.”
Is the quote from one of our survey takers.

A strong majority are showing that keeping up with given medication and sticking to a low sodium diet are helping with preventing their CKD from getting worse.

While others being treated with medication are wanting more one-on-one with dietitians to help improve quality of life. Many echo the same sentiment of fatigue in day-to-day tasks, as others cannot afford to take a day off work to get treatment, because they can’t afford rent and healthcare.

“*My husband does peritoneal dialysis every night and I set up the machine for him because he is blind. He is on a special diet because of his health issues. We no longer travel. He does regular blood work and medical appointments. Every 4 weeks we get a very large medical supply delivery. We know what day it's coming but not what time. We have had the shipment arrive as late as 8:00 p,m. so obviously we cannot plan anything on those days. The supplies take up the better part of an entire room in our house.”*

Improved Outcomes

More knowledge from their given medical practitioner to the client is what is most being repeated. The more information is kept from them the worse they feel about their condition. Even taking precautionary measures, like making sure people are getting tested for CKD so people don’t end up like this quoted couple.
“My spouse's CKD was a result of untended type 2 diabetes. In saying that, not enough warning is given to patients regarding the possible fatal consequences of long tern diabetes and high blood pressure. We had no idea that he would loose his eyesight due to the diabetes. And had not a clue about kidney disease.”

Experience With Drug Under Review

I use it to treat hypertension and it has been working well form many years. I am also a pre-diabetic. In addition, I have sufficient knowledge of hypertension and diabetes to take measures in daily living to ensure mitigation of potential areas of disease progression are optimized. what is not working well is my physician not providing me with my lab values report.

Most are saying that due to constant check ups in the ballpark of every six months they are not suffering from any noticeable decline.
We asked if you were asked to switch to a generic, most said that they were always on a generic medication because of OHIP coverage. Others that had switched had no noticeable change in the medication not living up to its named branded counterpart. Even some saying they've switched off it because of the "filler" in the medication.

Companion Diagnostic Test

We did not ask for specifics in biomarker testing we did ask "Thinking of your experience with CKD diagnosis and management,which option below needs improvement?"

30% of respondents answered "Earlier testing for kidney function"
With results ranging from people who are in severe late stages of CKD and to those who had blood tested but no urine tests.

With one respondent even making a list:

- *Ongoing community support*

- *financial support for dialysis and related costs of this treatment- medication coverage 100% for this chronic condition*

- *ongoing education on prevention*

We also asked Which SGLT2 inhibitor do you take (Dapagliflozin was only 9 people.) With the follow up, "what's working well, what's not working well."
With scary responses like "*Nothing is working well right now. Was diagnosed in 2004 and have had good results from medications but it seems like now at the age of 74 not responding to medication."*

It seems like even though people are living with this that they are not getting the information and testing they need.

Anything Else?

We also asked "In addition to CKD, do you or your loved one (with CKD) suffer from any condition listed below?"

ANSWER CHOICES		RESPONSES	
Pre-diabetes		7.35%	5
Type 2 diabetes		39.71%	27
High blood pressure		54.41%	37
High cholesterol		17.65%	12
Kidney disease		36.76%	25
Heart disease (previous heart attack or stroke)		19.12%	13
Heart failure h. cancer (all forms)		4.41%	3
Other (please specify)	Responses	27.94%	19
Total Respondents: 68			

Pre-diabites	7.35%
Type 2 diabetes	39.71%
High blood pressure	54.4%
High cholesterol	17.65%
Kidney disease	36.76%
Heart disease (previous heart attack or stroke)	19.12%
Heart failure h. cancer (all forms)	4.41%

Patient Group Conflict of Interest Declaration - CARP

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   We only used in house representatives.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   We used Surveymonkey to create the survey and our own means to publish it.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review:

   We as an advocacy group have worked with many different companies over the past 2 years.
   And have recently worked on a unbranded kidney campaign with the aims to inform people about getting tested.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AstraZeneca Canada		$7500 to finance the survey		

Clinician Input

BC Renal Medical Directors on behalf of provincial nephrologists

About the BC Renal Medical Directors

The BC Renal Medical Directors represent 66 practicing nephrologists within the province of BC. There are multiple MD subgroups, the largest of which is the The BC Consensus Group which includes all BC nephrologists who are practicing in British Columbia, and is voluntary. That group is committed to enabling equitable access to best evidence informed practices for patients living with kidney diseases.

BC Renal is an organization, funded by the MOH, which is responsible for standards, guidelines and also stewarding of the funding allocated for kidney care in the province. MOH funds all aspects of kidney care in the province, as part of this provincial body, excluding MD fees. Members of BCR include MDs, nurses, pharmacists and patients. There are committees including the Medical Advisory Group, and Pharmacy Formulary Committee who are heavily involved in multiple activities. The Medical Directors are the Physician leads for the five geographical health authorities, responsible for ensuring that the principles, practice and policies of BCR are implemented to ensure best outcomes for patients.

Information Gathering

Regular communication between the MDs and other clinicians occurs via committees.

Information from published literature, abstracts, as well as a local analysis using provincial data was reviewed for the purposes of this submission.

Current Treatments and Treatment Goals

Chronic Kidney Disease (CKD) affects 1:10 Canadians, and is associated with high burden of hospitalizations, resource utilization, cardiovascular events and costs to the health care system. Current therapy for CKD, prior to dialysis, is aimed at delaying progression of CKD, and addressing complications associated with decline including anemia, metabolic bone disease, hyperuricemia, electrolyte disorders acidosis and heart failure, and accelerated atherosclerosis. Current treatments include ACEi, ARB, and other antihypertensive, use of potassium binders and sodium bicarbonate as indicated, and hypouricemic drugs. Diet and exercise as well as addressing health literacy, education and mental health impact of chronic conditions are also offered within the context of nephrology practices and multidisciplinary teams. The current medication armamentarium addresses some of the components of progressive CKD, but not all, and are only modestly effective (e.g., RR 16% of ARB for dialysis prevention over 3 years in those with advanced diabetic CKD). Some of the other medications (iron, ESA target Hb and its associated fatigue/ cognitive impairment, exercise intolerance), whilst others alleviated other conditions (HTN, gout etc.). Heart failure is managed with conventional therapies, including diuretics, ACEiARB, beta blockers and nitrates. Some patients with CKD are intolerant of those therapies.

The costs of dialysis in Canada is approximately 100K$ per patient year, inclusive of medications, but exclusive of MD fees, hospitalizations, and out of pocket expenses for patients and families. Resource utilization for patients as they approach kidney failure, increases (hospitalizations for kidney related and unrelated conditions (e.g. MI, HF). Note that there is variability in CKD progression between individuals, with respect to rate of change, in part impacted by inter-current events, and in part due to intrinsic nature of the specific cause of CKD.

The goal of ideal therapies would be to delay progression (or arrest it) of CKD and its attendant complications, in particular Cardiovascular events (MI, Heart failure), and prolong dialysis free life and hospitalizations.

Treatment Gaps (unmet needs)

Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Current therapies do not reliably delay progression in all individuals, and not all individuals are able to tolerate current therapies (e.g. ACEi, ARB), which are the cornerstones of therapy. Excessive monitoring of these agents is also required. The relative risk reduction of current therapies is modest, in comparison to the SGLT2i group (16 vs 30%).

The current treatments do not consistently address key outcomes (CVD, delay of dialysis, hospitalization). Treatments that are well tolerated, accessible, and simple to use are needed. Once a day therapies have been shown to improve adherence and limit pill burden, which is already high.

Place in Therapy

How would the drug under review fit into the current treatment paradigm?
The current mechanisms by which SGLT2i impact outcomes are varied and multiple: through hemodynamic moderation, alteration of metabolism, reduction in total body sodium and water, weight loss and uric acid excretion: all of these would impact and complement existing therapies, or offer novel mechanisms by which progression of CKD is impacted. Data from RCT demonstrate reduction of BP, weight, uric acid, improvement in heart failure symptoms and hospitalization, and attenuation of GFR decline.

The drug could be used as first line or in combination with other medications, depending on circumstances. Majority of studies have demonstrated value in combination with established therapies; although there are data suggesting similar effects of these agents when used without RAS inhibition.

The drug would be recommended in those patients with CKD at risk of progression or CVD events.

The current treatment paradigm would certainly shift, to the benefit of patients and the health care system.

The drug would be in addition to current medications (as tolerated) and in some instances would permit reduction or cessation of other medications (e.g. Diuretics, potassium binders, uric acid lowering medications), which would be valued by patients and payers.

Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?
Current clinical trial evidence across multiple patient populations with CKD (early and later stage) and those with heart failure and modest CKD, describe the value of this medication in those groups.

Those with uACR > 20 and eGFR >25 are best studied, but there is new data to be available in Fall 2022 for non proteinuric CKD, with eGFR 20-45 which would inform further broadening.

There are no issues with dx of CKD in this area, but there are some individuals who are underdiagnosed (i.e. + UACR but normal eGFR).

The patient groups enrolled in studies were broad, and international: the benefit appears to be consistent across all subgroups.

What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?
The outcomes in clinical practice (uACR, change in eGFR, hospitalization for heart failure) are the same ones used in clinical trials.

Clinically meaningful response to treatment includes a plateauing of kidney function per 4-8 months, usually with a reduction in proteinuria. Other responses include lowering of Uric acid, weight loss and reduction of BP. Reduction in heart failure symptoms and hospitalizations would also be seen.

Monitoring of these individuals and the specific parameters is standard of care both in primary and specialty clinics, no extra burden on the health care system would be required.

What factors should be considered when deciding to discontinue treatment with the drug under review?
Recurrent untreatable mycotic genital infections; intolerable urination frequency, or episode of Diabetic ketoacidosis (only in diabetics).

All of these are rare events.

What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Community setting, primary care physicians and specialist clinics (nephrology, cardiology, internal medicine).

Specialists not essential but may be valuable with those with lower GFR values.

Additional Information

There is overwhelming clinical trial data based on international studies of 4000- 12000 pts, which are consistent over time, specific agent (cana, dapa and empa), and 3 dedicated trials in those with kidney disease, which describe a 30% relative risk reduction in important clinical outcomes, on top of best current therapy. SGLT2i delay progression of important outcomes of relevance to patients and to the health care system, and should be available to all who would benefit. They are easy to use, and all studies used fixed doses, so titration and other processes are simplified for practitioners and patients.

We attach here a provincial analysis of potential cost savings to the health care system for those under the care of nephrologists

This has been submitted for publication, and another more detailed economic analysis is in preparation.

This submission has been endorsed by the five Medical Directors of all geographical Health Authorities, representing 66 practicing nephrologists, who care for approximately 18,000 CKD patients in the context of offices or multidisciplinary clinics.

Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

On the steering committee for CREDENCE, and EMPA KIDNEY, and participated as PI or national lead in CREDENCE, DAPA CKD and EMPA Kidney; she has given talks on SLGT2i for national and international meetings. Payment for any activities has been donated to Pacific Nephrology Group, and UBC Educational Fund.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   NO

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   NO

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Adeera Levin
Position: UBC Professor of Medicine, Head Division of Nephrology. BC Renal Executive Director
Date: 20-07-2022

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen	x			
AstraZeneca	x			
Boeingher Ingleheim	x			

Declaration for Clinician 2

Name: Dr Melanie Brown
Position: Medical Director Fraser Health Authority Renal Program
Date: 08-08-2022

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 3

Name: Dr. Michael Copland
Position: Sr Medical Lead, BCR, Medical Director Vancouver Coastal Health/ Providence Health Care Renal Program, and Provincial Lead Home Hemodialysis
Date: 08-08-2022

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 4

Name: Dr John Antonsen
Position: Sr Medical Lead BC Renal Quality and Safety, Provincial Lead Hemodialysis
Date: 08-08-2022

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 5

Name: Dr Marie Michaud
Position: Medical Director Interior Health Authority Renal Program
Date: 08-08-2022

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 6

Name: Dr Anurag Singh
Position: Medical Director Northern Health Authority Renal Program
Date: 08-08-2022

Table 6: Conflict of Interest Declaration for Clinician 6

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 7

Name: Micheli Bevilacqua
Position: Chair, BC Renal Provincial Kidney Care Committee
Date: 16-08-2022

Table 7: Conflict of Interest Declaration for Clinician 7

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen	x			

AstraZeneca	x			

The Nova Scotia Health Authority Renal Program

About Your Clinician Group

The clinician group for this submission is comprised of nephrologists, internal medicine physician and a pharmacist at Nova Scotia Health. Please see the following link regarding renal services provided to the province of Nova Scotia.
https://www.nshealth.ca/renal/renal-programs-and-services

Information Gathering

Collaboration with key expert stakeholders within Nova Scotia Health Renal, Internal Medicine and Pharmacy and an extensive search of primary literature and national/international guidelines was conducted.

Current Treatments and Treatment Goals

As you are aware, dapagliflozin received a Health Canada indication on August 6, 2021 to reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular and renal death in adults with chronic kidney disease, **irrespective of whether or not they had diabetes**. This is monumental for the nephrology and internal medicine community in that a treatment that was originally felt to be limited to diabetes management, has benefits that extend far beyond.

There have been two completed trials that have studied the benefit of SGLT2 inhibitors among individuals with chronic kidney disease namely, CREDENCE and DAPA-CKD. CREDENCE focused on diabetic kidney disease (DKD) whereas DAPA-CKD included both DKD and non-DKD patients. The main inclusion criteria for DAPA-CKD were an eGFR 25-75 ml/min/1.73m2, and ACR > 20 mg/mmol and for CREDENCE were an eGFR 30-89 ml/min/1.73m2, ACR > 30 mg/mmol and AIC 6.5-12%.

The key findings of DAPA-CKD cannot be overstated. In this trial, the number needed to treat to prevent one primary outcome event (sustained decline in eGFR of at least 50%, end-stage kidney disease or death from renal or cardiovascular causes) was **19** over a median of 2.6 years. This was despite the fact that 98% of patients were already receiving standard of care with angiotensin receptor blockade (ARB) or angiotensin converting enzyme (ACE) inhibitor blockade. Furthermore, all-cause mortality was also statistically significantly in favor of dapagliflozin compared to placebo. The effects of dapagliflozin were similar in participants with or without type 2 diabetes and the known safety profile of dapagliflozin was confirmed.

The ideal treatment goals with dapagliflozin are to delay kidney disease progression necessitating renal replacement modalities (i.e. dialysis, renal transplantation), delay development of kidney disease complications, improve health-related quality life to enable greater life participation, and maintain employment and independence.

Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL,Charytan DM et al. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. N Engl J Med 2019; 380:2295-2306. https://doi.org/10.1056/NEJMoa1811744

Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al. N Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med 2020; 383:1436-46.
https://doi.org/10.1056/NEJMoa2024816

Treatment Gaps (unmet needs)

Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments

There has been no new treatment for over 20 years for diabetic kidney disease (DKD) or non-DKD since the advent of disease modifying therapies, angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs). With ACE inhibitors

and ARBs, as kidney function declines, the development of hyperkalemia can lead to suboptimal dosing of ACE inhibitors/ARBs and reduced benefit.

The above goal of delaying kidney disease progression necessitating dialysis has both patient and health care system benefits. Mathematical modeling has suggested that dialysis may be delayed up to 13 years based on an average patient treated with an SGLT2 inhibitor such as dapagliflozin. While the inclusion of dapagliflozin on the provincial formulary may increase drug costs, it is important to factor in the high yearly cost of dialysis and its complications along with patient benefits of delaying dialysis. To put this in perspective, the average annual cost of dialysis approximates 80,000 CAD. **Delaying dialysis for 13 years would save between 500,000-1,000,000 dollars per treated patient.** Thus, the overall cost savings of making this medication widely available to eligible Nova Scotian patients with chronic kidney disease is clear.

Durkin M, Blais, J. Linear Projection of Estimated Glomerular Filtration Rate Decline with Canagliflozin and Implications for Dialysis Utilization and Cost in Diabetic Nephropathy. *Diabetes Ther* 2021; **12:** 499–508. https://doi.org/10.1007/s13300-020-00953-4

Treatment with dapagliflozin is a convenient daily oral therapy and has been shown to be tolerated well.

Place in Therapy

How would the drug under review fit into the current treatment paradigm?

Recommend dapagliflozin as a first-line treatment for Diabetic Kidney Disease and Non-Diabetic Kidney Disease for patients meeting the inclusion criteria outlined in DAPA-CKD trial (Under Point 3. Above) in conjunction with ACE inhibitor/ARB therapy.

The leading hypothesis of the combined effects of SGLT2 inhibition and ACE inhibitors /ARBs on intraglomerular pressure has the potential for additive hemodynamic benefits and potential for long-term renal protection.

Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Adults with or without type 2 diabetes who have an estimated glomerular filtration rate (eGFR) of 25 to 75 ml per minute per 1.73 m2 of body-surface area and a urinary albumin-to-creatinine (UACR) ratio > 20 mg/mmol would be best suited for dapagliflozin 10 mg po daily. See Point 3. Above and hyperlink below:

Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al. N Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med 2020; 383:1436-46.
https://doi.org/10.1056/NEJMoa2024816

What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Stabilization or slowed decline in eGFR and or UACR.

Reduction is severity of symptoms and ability of greater life participation from reduced proteinuria (i.e. edema).

Consider yearly assessment of treatment response for stable patients.

What factors should be considered when deciding to discontinue treatment with the drug under review?

While an initial eGFR is expected with initiation of dapagliflozin, some clinicians may conduct other evaluations and reassess SGLT2 therapy if greater than 25% decline in eGFR upon initiation of dapagliflozin.

Significant volume depletion due to acute illness may require temporary discontinuation. Sick day management is important to provide to all patients. Dapagliflozin my need to be withheld during times of surgery.

If risk of hypotension/hypovolemia, consider decrease in blood pressure and diuretic medications (as applicable) prior to initiating dapagliflozin.

For additional clinical scenarios and associated management, See KDIGO 2020 Clinical Practice Guidelines for Diabetes Management and Chronic Kidney Disease. Kidney Intern 2020; 98 (45); S1-120. https://kdigo.org/wp-content/uploads/2020/10/KDIGO-2020-Diabetes-in-CKD-GL.pdf

What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

All health care settings managing patients with chronic kidney disease including primary care, hospital (outpatient clinics), specialty clinic would be appropriate for dapagliflozin management. While a specialist is not deemed a requirement to diagnose, treat and monitor patients on dapagliflozin, it may be identified during a specialist visit that a patient with chronic kidney disease is not on dapagliflozin and as such would potentially initiate treatment collaboratively with primary care family physician (if they have one). The type of specialist would include: nephrologist, internal medicine physician, endocrinologist and cardiologist.

Additional Information

We are hopeful that this new evidence of dapagliflozin's efficacy and safety will result in a positive CADTH review and will support the inclusion of dapagliflozin on the Nova Scotia Pharmacare Drug Formulary for patients with chronic kidney disease in the future. Thank you again for your support and we will gladly provide you with anything further you may require.

Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Declaration for Clinician 1

Name: Dr. Steven D Soroka
Position: Professor of Medicine, Dalhousie University and Senior Medical Director, Renal Program and Pharmacy
Date: 02-08-2022

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		X		
Jansen	X			

Declaration for Clinician 2

Name: Dr. Karthik Tennankore
Position: Associate Professor, Department of Medicine, Division of Nephrology, Dalhousie University
Consultant Nephrologist, Nova Scotia Health, QEII Foundation Endowed Chair in Transplantation Research
Date: 09-08-2022

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca	X			

Declaration for Clinician 3

Name: Dr. Penelope Poyah
Position: Associate Professor of Medicine, Department of Medicine, Dalhousie University
Medical Lead Nova Scotia Health Central Zone Renal Clinic
Date: 02-08-2022

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 4

Name: Dr. Michael Mindrum
Position: Assistant Professor, Department of Medicine, Dalhousie University, Internal Medicine, Valley Regional Hospital, Nova Scotia Health
Date: 09-08-2022

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 5

Name: Dr. Jo-Anne Wilson
Position: Clinical Pharmacy Specialist/Coordinator NSH Renal Program, Associate Professor, Dalhousie University
Date: 02-08-2022

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Industry Input

AstraZeneca Canada

Does the proposed project scope accurately reflect the treatment landscape?

Yes we agree with the project scope.

Are you aware of relevant published studies that you would like considered in the clinical review?

	Study
DAPA-CKD	Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2020;383(15):1436-1446. PubMed
CADTH DAPA-CKD Rapid Review with Expert Input	Zheng RJ, Wang Y, Tang JN, Duan JY, Yuan MY, Zhang JY. Association of SGLT2 inhibitors with risk of atrial fibrillation and stroke in patients with and without type 2 diabetes: a systemic review and meta-analysis of randomized controlled trials. J Cardiovasc Pharmacol. 2021;22:22. PubMed
	Kelly MS, Lewis J, Huntsberry AM, Dea L, Portillo I. Efficacy and renal outcomes of SGLT2 inhibitors in patients with type 2 diabetes and chronic kidney disease. Postgrad Med. 2019;131(1):31-42. PubMed
	Chertow GM, Vart P, Jongs N, et al. Effects of Dapagliflozin in Stage 4 Chronic Kidney Disease. Journal of the American Society of Nephrology. 2021;32(9):2352-2361. PubMed
	Heerspink HJL, Cherney D, Postmus D, et al. A pre-specified analysis of the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) randomized controlled trial on the incidence of abrupt declines in kidney function. Kidney International. 2021;22:22. PubMed
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	Heerspink HJL, Sjostrom CD, Jongs N, et al. Effects of dapagliflozin on mortality in patients with chronic kidney disease: a pre-specified analysis from the DAPA-CKD randomized controlled trial. European Heart Journal. 2021;42(13):1216-1227. PubMed
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	McMurray JJV, Wheeler DC, Stefansson BV, et al. Effect of Dapagliflozin on Clinical Outcomes in Patients With Chronic Kidney Disease, With and Without Cardiovascular Disease. Circulation. 2021;143(5):438-448. PubMed
	McMurray JJV, Wheeler DC, Stefansson BV, et al. Effects of Dapagliflozin in Patients With Kidney Disease, With and Without Heart Failure. JACC Heart Fail. 2021;9(11):807-820. PubMed
	Persson F, Rossing P, Vart P, et al. Efficacy and Safety of Dapagliflozin by Baseline Glycemic Status: A Prespecified Analysis From the DAPA-CKD Trial. Diabetes Care. 2021;44(8):1894-1897. PubMed
	Wheeler DC, Jongs N, Stefansson BV, et al. Safety and efficacy of dapagliflozin in patients with focal segmental glomerulosclerosis: A prespecified analysis of the DAPA-CKD trial. Nephrology Dialysis Transplantation. 2021;25:25. PubMed
	Wheeler DC, Stefansson BV, Jongs N, et al. Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol. 2021;9(1):22-31. PubMed
	Wheeler DC, Toto RD, Stefansson BV, et al. 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 International. 2021;100(1):215-224. PubMed

	Cherney DZI, Dekkers CCJ, Barbour SJ, et al. Effects of the SGLT2 inhibitor dapagliflozin on proteinuria in non-diabetic patients with chronic kidney disease (DIAMOND): a randomised, double-blind, crossover trial. Lancet Diabetes Endocrinol. 2020;8(7):582-593. PubMed
	Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2020;383(15):1436-1446. PubMed
	Lin YH, Huang YY, Hsieh SH, Sun JH, Chen ST, Lin CH. Renal and Glucose-Lowering Effects of Empagliflozin and Dapagliflozin in Different Chronic Kidney Disease Stages. Front Endocrinol (Lausanne). 2019;10:820. PubMed
	Pollock C, Stefansson B, Reyner D, et al. Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2019;7(6):429-441. PubMed
	Fioretto P, Del Prato S, Buse JB, et al. Efficacy and safety of dapagliflozin in patients with type 2 diabetes and moderate renal impairment (chronic kidney disease stage 3A): The DERIVE Study. Diabetes Obes Metab. 2018;20(11):2532-2540. PubMed
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	Chertow GM, Vart P, Jongs N, et al. Effects of Dapagliflozin in Stage 4 Chronic Kidney Disease. Journal of the American Society of Nephrology. 2021;32(9):2352-2361. PubMed
DECLARE	Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. Diabetes Obes Metab. 2018 Nov;20(11):2532-2540. PubMed
	Zelniker TA, Raz I, Mosenzon O, et al 2021- Effect of Dapagliflozin on Cardiovascular Outcomes According to Baseline Kidney Function and Albuminuria Status in Patients With Type 2 Diabetes A Prespecified Secondary Analysis of a Randomized Clinical Trial. JAMA Cardiol. 2021 Jul 1;6(7):801-810. PubMed
	Mosenzon O, Wiviott ST, Cahn A, et al. Effects of dapagliflozin on development and progression of kidney disease in patients with type 2 diabetes: an analysis from the DECLARE-TIMI 58 randomised trial. Lancet Diabetes Endocrinol. 2019 Aug;7(8):606-617. PubMed

Do you have additional comments that you feel are pertinent to this review?

- Health Canada issued a Notice of Compliance on August 10, 2021 for the following indication: **FORXIGA is indicated to reduce the risk of sustained eGFR decline, end-stage kidney disease, and cardiovascular and renal death in adults with chronic kidney disease (CKD).**[1] This indication was reviewed through Health Canada's Priority Review Process, which is reserved for drugs that have shown substantial evidence of clinical effectiveness for a serious, life-threatening, or severely debilitating disease or condition for which no drug is presently marketed in Canada or for a drug that provides a significant improvement over currently available options in Canada.[2]

- After reviewing the "Dapagliflozin for Chronic Kidney Disease Rapid Review with Expert Input", we wanted to bring forward 3 points for CADTH's consideration:

    1. In reference to the callout on the lack of statistical significance in specific subgroup analyses,[3] we wanted to highlight that the DAPA-CKD trial was not specifically powered for those subgroups alone.[4,5,6] Should specific subgroup analyses be required, results should be looked at with respects to how they compare to the overall population. Here is an explanation using the stage 4 CKD:[4]

        - The prespecified subgroup analysis of the DAPA-CKD trial based on CKD stages (stage 4 and stage2/3) showed beneficial effects of dapagliflozin on kidney and cardiovascular end points in patients with stage 4 CKD, similar in magnitude to the larger group of patients with stages 2/3 CKD.[4]

        - More specifically, the interaction p-values for the primary endpoint, end stage kidney disease (ESKD) endpoint, and all-cause death endpoint in the stage 4 CKD patient group were 0.22, 0.64, 0.95 respectively,

indicating that the outcomes for the stage 4 CKD patient group is no different from the stage 2/3 CKD patient group, and overall patient population.[4]

A similar review can be done for other subgroups mentioned in the rapid review such as the normoglycemic [5] and ischemic and hypertensive [6] patients where results were similar to overall population with no significance in the interaction p-values.

Furthermore, understanding that these sub-analyses are limited by their small number of clinical events, we can also look at the examined eGFR slopes as an intermediate outcome (a surrogate for large decrements in kidney function or incidence of kidney failure), showcasing that patients randomized to the dapagliflozin arm in each sub-analysis demonstrated attenuation in chronic eGFR decline.[4,5,6]

2. While the DAPA-KCD trial was FORXIGA vs placebo, both the placebo and dapagliflozin arms were composed of CKD patients on standard of care therapy (i.e angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB)).[7] Therefore, FORXIGA may not have been directly studied versus ACEi or ARBs as mentioned in the limitation section of the rapid review,[3] though it does have substantial evidence on top of standard of care (i.e ACE/ARBs).

   Furthermore, dapagliflozin consistently reduced the risk of the primary and secondary outcomes, regardless of baseline ACEi/ARB dose level. Here as well, interactions p-values for these sub-groups were not statistically significant inferring that subgroup results were similar to the overall patient population.[8]

3. Lastly, we want to inform CADTH of multiple health economic publications/reviews from DAPA-CKD that fell out of the rapid review scope. As per below table, several have been published (manuscripts and posters), and others are yet to come. Key HTA markets have also reviewed this file (NICE,[9] SMC [10] and ZIN[11]) and have all concluded that FORXIGA was shown to be cost effective or highly-cost effective.[9,10,11]

   As you review these documents, we thought pertinent to emphasize that ESKD, especially dialysis, are among the most costly complications encountered by any healthcare system; with the annual per patient cost rising exponentially between CKD stage 3 and dialysis. [12]

   Dapagliflozin has shown, after 20 years of little innovation in this field, a substantial and statistically significant reduction in ESKD. The number of participants who needed to be treated during the trial period to prevent one primary outcome event was 19 (95% CI, 15 to 27); which was remarkably low, demonstrating the good value for money. [7]

   ESKD events take some time to take place for patients who start the analysis at CKD stage 3 or earlier, hence, budget impact starts to become highly favourable after the first 3-5 years. It is important for patients and clinicians to be able to act early to protect their patients from poor cardiorenal outcome.[13]

   Additional information on the high burden of CKD and Renal Replacement Therapy (RRT) could be leveraged using the incidence of RRT from INSIDE CKD. This burden has increased considerably due to COVID which has put nephrology services at additional strain through an increased incidence of acute kidney injuries, higher need for dialysis treatment and fewer renal transplants being performed.[14]

Study	**Publication details**
McEwan P, Darlington O, Miller R, et al. Cost-effectiveness of dapagliflozin as a treatment for chronic kidney disease: a health-economic analysis of DAPA-CKD	To be published in CJASN imminently
McEwan P, Darlington O, Miller R, et al. Translating the findings of DAPA-CKD to reductions in healthcare resource utilization from a US payer perspective. JMCP *Presented at AMCP 2021, Virtual meeting, 12 April 2021 –16 April 2021*	Poster available (Abstract ID: 976229) Publication Fall of 2022

McEwan P, Darlington O, Boyce R, et al. Estimating the impact of delayed disease progression and cardiovascular event incidence associated with dapagliflozin based on the results of DAPA-CKD. JMCP *Presented at AMCP 2021, Virtual meeting, 12 April 2021 –16 April 2021*	Poster available (Abstract ID: 976324) Publication Fall of 2022
Mennini FS, Cabrera C, Card-Gowers J, et al. Inside CKD: projecting the economic burden of chronic kidney disease using patient-level microsimulation modelling. Value Health *Presented at virtual ISPOR Europe 2021, 30 November–3 December 2021*	Poster from ISPOR available (POSB68) *Captures Canada*

- Chronic kidney disease is associated with a significant clinical burden in patients, encompassing substantial morbidity and mortality, even in early stages of disease, and this risk increases as CKD progresses. CKD has significant physical, social, emotional, work and financial impacts on both patients and carers, see below poster for more details. Access to FORXIGA will improve patient and carer quality of life (QoL).[15]

Study	**Publication details**
Sanchez JJG, Kularatne T, West Bronwyn, et al. PaCE CKD: impact of CKD on patients and carers – qualitative insights from a series of multinational interviews. Science Direct *Presented at the International Society of Nephrology's World Congress of Nephrology 2022, 24–27 February 2022*	Poster Available (WCN22-0774)

- As mentioned in the health economics section above, it is important for customers to act early to protect their patients from cardiorenal outcomes. Access to FORXIGA for CKD patients is important and will have limited budget impact to drug plans as generics will enter the market following FORXIGA's loss of exclusivity in May 2023.

References:

1. AstraZeneca Inc. FORXIGA Product Monograph Product Monograph, August 6th 2021
2. Health Canada. Guidance for Industry – Priority Review of Drug Submissions. Health Canada
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4. Chertow GM, Vart P, Jongs N, et al. Effects of Dapagliflozin in Stage 4 Chronic Kidney Disease. Journal of the American Society of Nephrology. 2021;32(9):2352-2361. PubMed
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7. Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2020;383(15):1436-1446. PubMed
8. Heerspink HL, Jong N, Stefansson B, et al. Effect of dapagliflozin in patients with chronic kidney disease according to background angiotensin-converting enzyme inhibitor and angiotensin receptor blocker dose. ERA *Presented at 59th ERA congresss: May 19-22, 2022*

9. National Institute for Health and Care Excellence: Single Technology Appraisal: Dapagliflozin for treating Chronic Kidney Disease. 2022. NICE

10. Scottish Medicines Consortium: Advice on New Medicine: dapagliflozin 10mg film-coated tablets (FORXIGA). 2022. SMC

11. Zorginstituut Nderlands : GVS advice dapagliflozin (FORXIGA) extension of further condition. 2021. ZIN

12. Norhammar A, Bodegard J, Eriksson JW, et al. Cost of healthcare utilization associated with incident cardiovascular and renal disease in individuals with type 2 diabetes: A multinational, observational study across 12 countries. 2022; 24(7):1277-1287. PubMed

13. McEwan P, Darlington O, Boyce R, et al. Estimating the impact of delayed disease progression and cardiovascular event incidence associated with dapagliflozin based on the results of DAPA-CKD. JMCP *Presented at AMCP 2021, Virtual meeting, 12 April 2021 –16 April 2021*

14. Mennini FS, Cabrera C, Card-Gowers J, et al. Inside CKD: projecting the economic burden of chronic kidney disease using patient-level microsimulation modelling. Value Health *Presented at virtual ISPOR Europe 2021, 30 November–3 December 2021*

15. Sanchez JJG, Kularatne T, West Bronwyn, et al. PaCE CKD: impact of CKD on patients and carers – qualitative insights from a series of multinational interviews. Science Direct *Presented at the International Society of Nephrology's World Congress of Nephrology 2022, 24–27 February 2022*