

CADTH COMMON DRUG REVIEW

Patient Input

DAPAGLIFLOZIN (Forxiga)

(AstraZeneca Canada Inc.)

Indication: Heart failure with reduced ejection fraction

CADTH received patient input from:

Cardiac Health Foundation of Canada

Heart Failure Support Group of Manitoba

The HeartLife Foundation

April 22, 2020

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.

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 personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	<u>Forxiga (dapagliflozin)</u> Indications: Heart failure with reduced ejection fraction
Name of the Patient Group	Cardiac Health Foundation of Canada
Author of the Submission	████████████████████
Name of the Primary Contact for This Submission	████████████████████
Email	██
Telephone Number	████████████████████

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Response:

We've been getting Canadians moving since our inception, spearheading the Walk of Life campaign in 1984 and getting our country's blood pumping for over 30 years.

Founded as Marina Lodge in 1965 and newly re-branded as the Cardiac Health Foundation of Canada, we're a charitable organization proudly dedicated to keeping Canadians' hearts healthy, including both cardiac rehabilitation and advocacy for disease prevention and education. You could say we're all heart.

Walking is one of the best ways to improve cardiovascular health, and we strive to bring as much awareness as we can to the need for prevention. Proceeds from the Walk of Life events provide vital funds for cardiac rehab programs, equipment, and medical research as well as towards scholarships and invited lectures.

Today, the National Walk of Life campaign raises funds for more than 23 much-needed programs from coast to coast.

Our Mission: Prevention, Education, and Cardiovascular Rehabilitation. To promote and develop cardiac rehabilitation services including public education, primary and secondary prevention initiatives in reducing cardiovascular disease in Canada, and in promoting active recovery.

To learn more, you can visit our website at: <http://www.cardiachealth.ca/>.

We have also partnered with HeartLife Foundation who is creating a separate submission in addition to collaborating on this one. The HeartLife Foundation is Canada's first – and only – national patient-led heart failure organization. It is a Federal Charity aimed at raising public awareness of heart failure, engaging patients, families, and caregivers to provide education and support, facilitate access to the latest research, innovations, and treatments, and advocate better care for all.

Their Mission: We aim to empower patient voices to stimulate dialogue, advance understanding, improve access to treatments and research, raise heart failure awareness, and improve patient care in Canada. We aim to collaborate with partners in healthcare, government, and industry to establish a strong, critical voice for heart failure patients in Canada. For more information go to www.heartlife.ca

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Response

The information gathered for this submission was gathered through a questionnaire administered through Survey Monkey. The Cardiac Health Foundation of Canada designed the 7 question survey in collaboration with the Heart Life Foundation. It was then placed on the homepage of the Cardiac Health Foundation of Canada and advertised through social media channels. The questionnaire was launched on March 17th 2020.

The survey asked respondents about their experience with Heart Failure including whether they had ever been prescribed Forixga and if so, what their experience had been with this medication. A total of six questionnaires were completed between March 17th 2020 and March 20th 2020. Patients were also offered the opportunity to be interviewed. Those who agreed to be interviewed would be offered \$35 for their participation. None of the respondents indicated an interest in being interviewed.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Response: Heart Disease In Canada

In Canada, heart disease for women is the leading cause of death and the second leading cause of death overall. Ischemic heart disease is the most common form of heart disease, it is the first cause of life years lost, and the second leading cause of disability.

Annually 158,700 Canadians over the age of 20 years and older received a diagnosis of ischemic heart disease. Of these 63,200 had their first heart attack. Although Heart & Stroke identifies 50,000 individuals being diagnosed with Heart Failure the annual incidence(600,000) and total numbers may be much higher. The Government of Canada (2017) reported that 92,900 Canadian adults received a new

diagnosis of heart failure. Peter Munk Heart Failure Clinic also suggests that 1,000,000 Canadian are now living with Heart Failure.

Respondents Insights

Although we were not able to determine how long each individual had been living with Heart Failure, we did learn about the day to day effects. This particular condition impacts on the day to day activities of daily living.

All respondents indicated they had to cut back on activities of daily living and to reduce the types of things they used to do. One respondent indicated they have an inability and energy to do some of the most basic things of life. Others indicated a severe shortness of breathe and inability to engage in physical activities.

All participants are managing at least five medications daily for their heart failure condition. Some of these medications which have been prescribed for arrhythmias in addition to Heart Failure have severe side effects (amiodarone).

One respondent indicated they were not initially made aware that they were suffering from Heart failure. That person indicated when they were hospitalized for the second time they were informed then that they were suffering from Heart Failure.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines)

Respondent

Overall the patients who responded to the survey indicated they would like to be able to do day to day basic activities a little easier with less struggling to breathe.

Current Therapies

The therapies the patients are receiving appear to be largely related to their medication. None of the respondents have ever taken Forizga/Dapagliflozin. All appear to watch what they eat. A few of the respondents indicated they wanted some self management techniques that would help them with day to day living. One respondent indicated they had been taking cardiac rehabilitation which initially helped them. They have not been able to continue this going forward.

Cost

We did not ask respondents about costs and whether they could afford the medications they were on. With each person managing five medications daily the costs are probably high. If we had of been able to do interviews we would have tabled these questions at that time

Current Challenges

We suspect all respondents are struggling with side effects of medication. Most respondents identified that they experienced side effects with each medication that they were taking.

The struggle with continuing cardiac rehabilitation or even participating in cardiac rehabilitation is an ongoing issue. A recent study in France of Heart Failure patients found the participation rate for cardiac rehabilitation was 10%. We suspect this rate is probably similar for Canada. We do know from this same study that specialized adapted cardiac rehab programs for Heart Failure patients assisted them to breathe easier which would then assist with day to day living activities.

One respondent indicated that based on their current struggles with day to day living they would have had a DNR order on their charts.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Response:

Areas of Improvement:

As mentioned in previous sections, respondents wanted self management techniques that would help them with day to day living. Most wanted support to help them breathe easier and thus reduce periods of shortness of breathe.

We suggest that cardiac rehab programs specifically for Heart Failure patients be made available. These programs would reduce hospitalization. The HeartLife Foundation is doing an online webinar with the Heart & Stroke Foundation with a key topic being, exercise during Covid 19. This approach would be helpful on an ongoing basis.

From the one respondents response who was angry over the impact of Heart Failure (LVAD) on his/her life, it suggests that depression is an issue. This person is clearly angry over being kept alive and suggest they would have a DNR order if they went back to hospital. They suggest the need for mental health support. We do know that individuals who have had Bypass Surgery (CABG) suffer from depression and may in fact be suicidal at times. Many Heart failure patients end up on the heart transplant list. This may situate them to increased rates of depression.

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

Response:

We were not able to speak with any respondents who had experience with the drug under review

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

Response:

We were not able to speak with anyone who had been prescribed the drug under review

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Response:

There are currently 50 million Heart Failure patients around the world. Heart Failure is extremely costly due to increased hospitalizations, reduced quality of life including reduced or eliminated participation in the workforce. In Canada the Peter Munk Heart Failure Clinic suggest that 1,000,000 Canadians are living with Heart Failure. The drug which is under review has shown it reduces mortality, hospitalizations and reduced side effects. This co-transporter2 (SGLT2) inhibitor also shows less impact on kidney function while reducing hospitalization for worsening heart failure patients. We encourage you to make this drug Forixga/Dapagliflozin available for individuals living with Heart Failure. Any proven attempt to save lives with a proven treatment needs to be made available for individuals living with Heart Failure in Canada.

We recommend that Cadth review favourably this new medication in the fight to reduce hospitalization, to save lives and to increase day to day living ability of people living with Heart Failure in Canada.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, 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.

Answer: we consulted with Heart Life Foundation to review our proposed survey monkey questionnaire. We also sent this group results of the survey.

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.

Answer : 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.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Astra Zeneca for a Video Cardiac Stories of Survival			x	
Amgen Canada for a Video Cardiac Stories of Survival			x	
Boehringer Ingelheim Lilly Diabetes Alliance Public Education			x	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: John A Sawdon MSc.
 Position: Public Education & Patient Advocacy Director
 Patient Group: Cardiovascular Disease
 Date: April 13th 2020

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Forxiga (Dapagliflozin)
Name of the Patient Group	Heart Failure Support Group of Manitoba
Author of the Submission	████████████████████
Name of the Primary Contact for This Submission	████████████████████
Email	████████████████████
Telephone Number	██████████

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

The Heart Failure Support Group of Manitoba (HFSG) was established in 2011. Membership composed of patients with diagnosis of heart failure and their family members/caregivers.

The purpose of the group is to provide support, education, and the opportunity for heart failure clients and their families / caregivers to interact with others with similar situations. Members meet formally on a quarterly basis but also meet informally. The group activities include education sessions where speakers are invited on topics that are relevant to care of those with heart failure or relevant to caregivers, invited guests/ speakers to talk on topics relevant to members including current management for heart failure. There are also social networking and gathering.

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

The support group had 2 meetings where SGLT2 inhibitors and their role in the treatment of heart failure (HF) with or without diabetes were discussed. These meetings/ presentations were held on November 21, 2019 and February 6, 2020 in Winnipeg, Manitoba. We had about 30 people present on November 21, 2019 and 25 people present on February 6, 2020. Those present were

composed of patients and their primary care givers. There was only 1 member taking Dapagliflozin without diabetes who willingly shared the information. He has not experienced any potential effects. There were a couple of patients who shared the information that they were receiving sgl2 inhibitors other than dapagliflozin who were also not reporting any potential side effects. Those three patients were knowledgeable as to treatment indication and are satisfied with their treatment regimen. They encouraged their fellow members to speak to their care provider about the drug and to find out if they meet the criteria for using the drug especially those without diabetes. Majority of those who attended are over the age of 65. Main concern raised by attendees is lack of funding/ reimbursement for the dru

3. Disease Experience

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We know that there are over 600,000 Canadians suffer or had suffered from heart failure and the number is increasing. HF is associated with multiple emergency and hospital visits. Despite advances in therapies and prevention efforts, death rates remain high. There is high unmet need for new treatments to help lower the chance of dying from this condition as well as with repeated hospitalizations. Recently the Canadian cardiovascular Society made their recommendation in regards to the use of Dapagliflozin which is as follow:

We recommend SGLT2 inhibitors, such as dapagliflozin be used in patients with mild to moderate heart failure due to reduced left ventricular ejection fraction (LVEF \leq 40%) and *without concomitant Diabetes*, to improve symptoms and quality of life and to reduce the risk of hospitalization and cardiovascular mortality (**Conditional Recommendation; High-Quality Evidence**). CCS, 2019.

A member of our group was present during the Canadian Cardiovascular Congress in Montreal and learned about Dapagliflozin. We also had an expert diabetes nurse who explained to the group the role of SGLT2 inhibitors and the result of several clinical trials in SGLT2 inhibitors including the DAPA-HF study and enlightened us on their role in improving cardiovascular outcomes. Members were very optimistic in learning new potential treatment for HF.

Caregiver stress/ burden is all too familiar with members of the group. Caring for someone has benefits such as personal fulfillment knowing that you are helping someone but care giving is also associated with physical (fatigue, lack or interrupted sleep)), psychological (anxiety, depression) and financial burden. Stressors are often persistent such as recurrent emergency room visits and hospitalization of their loved ones. Add to that the financial burden of treatment and loss of wages. WE a;; know that there is no cure for heart failure but stabilization of condition and symptoms can dramatically improve the lives of HF patients and caregivers.

4. Experiences With Currently Available Treatments

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Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Most members are on triple therapy (Ace I or ARB, beta blockers and MRA) and some are on newer therapies such as ARNI (Entresto) and Ivabradine (Lancora) depending on their tolerance. Members are free to discuss their reaction to their medications if they feel comfortable during our meetings.

Barriers previously identified for accepting care providers' recommendations for treatment includes lack reimbursement by provincial Pharmacare, perceived side effects of the medications, lack of knowledge about potential benefits of the treatment, and multipharmacy " I am already taking too many medications". Concerns of patients and caregivers are usually mitigated by proper explanations on how the medication works, the benefits, potential side effects of the medication and what to do when experiencing potential side effects..

We understand that Dapagliflozin is in a pill form. It does not require additional testing than the usual heart failure routine blood test and no additional clinic visit is anticipated than the usual HF clinic visit.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

We are aware that there is no cure for heart failure and that treatments are geared towards reducing symptoms, reducing emergency room visits and hospitalizations, reducing mortality (living longer) and improve quality of life. In addition to that, we are looking for treatment that has less side effects or tolerable side effects. We hope for HF patients to be able to have better quality of life; that is to be able to breath easier, walk longer, and sleep better. With treatments providing such outcomes, it would be easier for HF patients and caregivers to live a fairly normal life.

It is hard to think about what we want for trade offs. Medications may affect people differently. Some may not tolerate this medication due to potential side effects. Trade offs will have to be on individual basis. What would work for one person, may not work on another.

6. Experience With Drug Under Review

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The member who was started on Dapagliflozin is paying for his medication. He has no additional insurance. The other 2 who were on another SGLT2 inhibitor met the exceptional drug criteria as they have diabetes and on 2 other diabetes drugs and therefore has 80 % coverage through provincial funding after their deductibles have been met.

Since this drug has not been approved for HF cardiovascular outcomes, and only 1 member is using it for that indication, the members are hopeful that the use of this drug, based on the DAPA-HF study, will improve their cardiovascular outcomes, reduce symptoms, reduce hospitalization, reduce death and improve the quality of lives of those suffering from HF. The members of the group hope that treatments indicated for heart failure including the triple therapy will improve their energy (functional capacity), improve quality of life, prevent hospitalization, live longer and have fewer side effects from their treatments.

Again, there are still high unmet needs for new treatment, this new drug may meet some of the unmet needs.

7. Companion Diagnostic Test

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- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

As far as testing, the members understand that there is no additional diagnostic test needed for this medication. For those with diabetes, it would be the routine test for their diabetes including self monitoring of their blood sugar.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

We, the members of the Heart Failure Support Group of Manitoba hope and want improved access to new therapies that may improve the lives of patients with HF and those we care for.

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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. NONE

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Estrellita Estrella-Holder
 Position: Co-founder and support for the group
 Patient Group: Heart Failure Support Group of Manitoba
 Date: April 10, 2020

Name of the Drug and Indication	Dapagliflozin - Heart failure with reduced ejection fraction
Name of the Patient Group	The HeartLife Foundation
Author of the Submission	[REDACTED]
Name of the Primary Contact for This Submission	[REDACTED]
Email	[REDACTED]
Telephone Number	[REDACTED]

1. About Your Patient Group

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Our Mission: We aim to empower patient voices to stimulate dialogue, advance understanding of patient needs, improve access to treatments and research, raise heart failure awareness, and improve patient care in Canada. Our organization collaborates with partners in healthcare, government, and industry to establish a strong, critical voice for heart failure patients in Canada.

Founded by Dr. Jillianne Code, a two-time heart transplant recipient, and Mr. Marc Bains, a heart failure survivor and transplant, we have a network of over 1000 patient and carers across the country. As a volunteer run organization, The HeartLife Foundation works with 15-20 patient and carer champions to administer service programs, support groups, workshop events, public awareness campaigns and government relations activities. In collaboration with Dr. Sean Virani, one of Canada’s leading heart failure specialists, thought leaders, and promoter of patient and family centred care, we endeavour to ensure that there is an open dialog including patients as partners with healthcare providers, government, and industry across Canada.

Website: www.heartlife.ca

Facebook: www.facebook.com/heartlifecanada

Twitter: www.twitter.com/heartlifecanada

Instagram: www.instagram.com/heartlifecanada

2. Information Gathering

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Patient perspective information was gathered by The HeartLife Foundation through an in-person workshop, online surveys using 'Survey Monkey' and Facebook, literature searches from peer reviewed publications, lived experiences of Canadian Patients and Family Carers, and one-on-one conversations with medical healthcare professionals.

In-Person Roundtable

The purpose of the roundtable was to gain insight into the challenges facing Canadians directly affected by heart failure. The roundtable included 17 patients and carers from 8 Provinces aged 34-67. Specific objectives of the roundtable included: 1. Discuss patient/caregiver first-hand experiences, outcomes and identify gaps in the care continuum and 2. Discover aspects of care that are most valued to patients and caregivers and determine if these aspects are being met. The roundtable was held in May 2019.

Online Survey

Utilizing Survey Monkey, links to the survey were shared through Facebook, Twitter and The Cardiac Health Foundation of Canada's website. In total, 7 individuals completed the survey which had 7 questions and was available from April 1, 2020 to April 15, 2020. Survey Limitations: The survey was results were limited and do not reflect the views and experiences of all Canadians affected by Heart Failure. The survey allows us to understand the views of those who were able to answer the survey at a particular point in time.

Lived Experience Interviews

The HeartLife Foundation conducted four lived experience interviews with patients and cares in Canada. Interviews were conducted with patients and family carers aged 33-56 and represented a current heart failure patient, a family carer, and two post heart transplant recipients.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Heart Failure in Context

An estimated 600,000 people are currently living with heart failure in Canada (Heart & Stroke Foundation, 2016). In their 2016 Report on the health of Canadians, the Heart & Stroke Foundation estimates that

50,000 Canadians are diagnosed with heart failure each year and this number is on the rise. Heart failure costs the Canadian healthcare system more than \$2.8 Billion dollars per year – with the majority of those dollars being spent on acute care. Research has shown that effective treatment improves clinical outcomes, prevents hospitalizations, increases patient self-efficacy for managing their condition, and overall quality of life. Despite these findings, there continues to be significant gaps in rate of drug approvals in Canada. Approval of proven treatments are paramount in helping patients self-manage their condition and live the quality of life they deserve.

Lives of patients with heart failure and their family carers dramatically change upon initial diagnoses. People with heart failure experience a wide range of physical, social and emotional challenges. Individual can be born with the disease, develop it throughout their adult lives, or be diagnosed in their later years. Symptoms of heart failure vary among patients. It is a condition that requires daily monitoring, adherence and vigilance on the part of the patient in order to control the delicate balance of symptoms. These symptoms include shortness of breath, extreme fatigue, low blood pressure, dizziness, edema and bloating. Many patients also have palpitations and arrhythmia as a result of the underlying etiology of the cause of their heart failure. Heart Failure has no cure and, if left untreated, will become progressively worse over time. Heart Failure is commonly associated with a variety of comorbidities, anxiety, depression, a decline in cognitive ability, and can have a negative impact on mental health.

Roundtable Findings:

The purpose of the roundtable session was to: gain insight into the key challenges facing Canadians directly affected by heart failure, prioritize the challenges, and identify the top three health care challenges and gaps to address. Representation of patients and carers included: BC, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, Newfoundland and Labrador. As you will note below, equal access to medication was paramount for patients and carers.

Responses were consolidated to the following key challenges and prioritized green (1st), yellow (2nd), red (3rd)

Diagnosis – time to diagnosis / misdiagnosis ✓✓✓
Equal access to care – medications, rehab, digital records etc. ✓✓✓✓✓✓✓✓
Multidisciplinary care ✓✓✓✓✓✓✓✓✓✓
Life after heart failure – quality of life ✓✓✓
Transition from diagnosis to home ✓✓
Transparency of processes – e.g. how do I get a copy of my records? ✓✓
Education and self-management – expectations, post-surgery ✓✓✓✓
Mental health support – patients & caregivers ✓✓✓✓✓✓✓✓✓✓
Understanding cognitive impacts – research needed ✓

The top 3 identified priorities, as voted on by the patient & caregiver participants, were:

1. Equal Access to Care – medication / rehab / digital records
2. Multidisciplinary Care
3. Mental Health Support – patients & caregivers

Survey Results:

Utilizing Survey Monkey, links to the survey were shared through Facebook, Twitter and The Cardiac Health Foundation of Canada’s website. Although responses are limited it is important to note the significant negative shift in daily life for individuals diagnosed with Heart Failure. Respondents indicated changes in daily life as the result of shortness of breath, low energy and fatigue. Questions and a selection of answers are below:

<p>Question 1: Please describe the ways in which living with Heart Failure affects or has impacted on your day to day life?</p> <p>Selection of Answers:</p> <p>“The major shift was in diet and activity for myself and entire family. We had to change the day to day activities and slow down.”</p> <p>“Inability to have energy to do some of the most basic daily activities of daily living.”</p> <p>“shortness of breath on activity, limited physical endurance & easily fatigued.”</p>
<p>Question 2: Can you list the medications that you take to manage Heart failure, please list including doses and side effects.</p> <p>All medications listed:</p> <p>Anticoagulant (Apixaban and Warfarin), Sacubitril/valsartan (Entresto), ACE inhibitor (Ramipril), Amiodarone, Bisoprolol, Furosemide (Lasix), Spironolactone, Digoxin, and Candesartan.</p>
<p>Question 3: Do you have experience using Forxiga?</p> <p>All Respondents Answered: No</p>
<p>Question 4: If you have taken Forxiga in HFrEF did this medication help improve your day to day management of Heart Failure?</p> <p>All Respondents Answered: No</p>
<p>Question 5: If you could change one thing to explore your day to day life living with Heart Failure, what would you change?</p> <p>Selection of Answers:</p> <p>“Increase in self-management tools and resources.”</p> <p>“Improved self-management techniques to improve quality of life on a day to day basis.”</p> <p>“Improve shortness of breath & activity endurance.”</p>

Question 6: Would you be available and agreeable to a telephone interview?

All Respondents Answered: No

Question 7: Please identify the greatest challenges you have faced since being diagnosed with Heart Failure?

Selection of Answers:

"Continue to exercise after cardiac rehab."

"Limited my activity day to day and reducing my work schedule."

"Being able to enjoy activities I love."

Lived Experience Interviews

Although heart failure cannot be cured, patients and carers have the opportunity to live a good quality of life if the disease is effectively managed. The right treatment plan along with support can help patients feel better and live longer.

NYHA Class I or II

While in NYHA Class I or II, symptoms could be mild to moderate most days which means that laying down to sleep requires one or two pillows to help you be able to breathe at night while sleeping. Sleep is often restless, and disturbed, but if congestion is controlled well with medication, fluid restriction, and a low sodium diet, resting is possible. A daily nap is not unusual in these stages. In terms of daily activity, with mild to moderate symptoms, doing basic house hold chores and working in a non-strenuous job is manageable – as long as the patient is careful to adhere to the daily regimen of medications, diet, fluid restriction, and ensure that they get the rest they need. Weekends are often spent napping and resting. With exposure to others in the workplace, many heart failure patients are quick to catch seasonal colds and flus, which can easily exacerbate and even worsen heart failure symptoms potentially leading to hospitalization. In addition, with any physical activity, patients in this class will often have to take frequent breaks, will tire easily, become short of breath on exertion, and have to be careful to avoid extreme weather conditions (hot/cold). Many patients find regular exercise challenging, and demoralizing, and often walking on flat surfaces for short distances is all they can manage. Symptoms change daily.

Patient Experience Aged 56: *I am 56 years old and I live with a congenital heart defect. I was operated on at the age of 7 when the physicians repaired a coarctation of the aorta. My parents and I were told that I was "fixed". I led a very active young adult life into my thirties with many ups and downs, two live births of children, one at 29 and the next at 34 years of age. Fast forward to turning 40 when the troubles all truly began for me. I found myself winded while doing any activity, tired all the time, legs and arms heavy. I worked part time but I found I was unable to do much more than work, come home and sleep, go back to work. At this time, a very good friend of mine suggested one day when I was complaining about the fact I was so tired and winded, "that it could be your heart." Famous last words! Within the ensuing 15 years, I have had many tests, many medications and four ablations. I got a call from my GP's office while on vacation the summer of 2015, they had done testing and sent the results to my GPs office, who were following up with a phone call with me as they were concerned about the results. I knew what they were*

going to say before they said it! My heart arrhythmias were back, my ejection fraction was low. Life again was on hold.

Patient Experience Aged 35: I lived with heart failure for 10 years. I was in complete shock when I received my initial diagnosis. I was 23, healthy, and entering my first career. Upon diagnosis I had no idea what heart failure was and how it would change my life. Upon diagnosis and through to 2018 my ejection fraction was between 10%-25%. Personally, it was most important for me to get back to a “normal” life. Unfortunately, “normal” was near impossible. I had multiple incidents when the condition prevented me from driving for a period of 6 months each. During these periods my activities included resting, resting, walking, and resting. During one period in 2014 I went into cardiac rest, had CPR for 9 minutes and was placed in an induced coma for 8 days. Although I overcame that hurdle, life over the next 4 years was not without its struggles. I experienced multiple periods of cardiac arrest, which, ultimately culminated in a failed ablation and a spot on the transplant list. Not the life I imagined throughout my twenties and early thirties. At present time, I am grateful to say I am two years post-transplant.

NYHA Class IV

Patients in NYHA Class IV are in end-stage heart failure. Essentially this means, that despite optimal medical therapy, maximum dosages of medications, the only remaining alternatives for treatment are high risk high cost surgical interventions including: Mechanical support including left ventricular assist devices (LVAD), and heart transplantation. Patients in NYHA Class IV are very sick. Medical therapies are failing as their heart muscle has deteriorated to the point that severe edema in the legs and abdomen, and congestion in the chest lead to many sleepless nights, often sitting up in a chair to rest. Breathing in a horizontal position feels more like choking, gasping for air. Many have described it as feeling like you are drowning. Daily activities are difficult and exhausting, leaving most patients to spend the majority of their time resting at home, living increasingly isolated lives. Cognitive impairments become more severe as a result of the lack of blood flow to the brain resulting in difficulty focusing, reading, carrying on conversations. Most severe patients are often assessed for their suitability for listing for a heart transplant at this stage, end of life discussions are had, and a left ventricular assist device is often placed as a bridge to transplantation.

Patient Experience Aged 44: It is difficult to try and I tell all the details of my story. I could discuss about how for most of my adult life I have suffered, how at 28 heart failure literally squeezed the life out of my body, how I struggled to breathe with what felt like a vice around my chest. That despite a stroke, multiple ICD shocks, a left ventricular assist device, severe GI bleeding, countless transfusions, 13 months on the transplant list, a heart transplant, 8 days in a coma with multi organ failure, delirium, and having to learn to feed myself and walk again – that I refused to die. In the world of chronic illness, people often speak of finding your ‘new normal’. Those who are in it now, will understand what I mean. But even if you have never been there I think you can probably imagine what it might be like to have something so profound happen to you that you need to readjust your horizon. Constantly needing to find a ‘new normal’. 2 years after my second transplant, three years after my first transplant, 14 years after my diagnosis I still wonder at the logic of this statement. What does that even mean? What is normal, anyway?

Impact on Carers

Caregivers play an integral role in the heart failure care continuum. The challenges of heart failure on caregivers and family members cannot be understated. Caregivers provide support, guidance, attend appointments, track medications, monitor symptoms, and are often the first point of contact with the healthcare team. The lives of caregivers can be as unpredictable as the patient. They have to make

drastic life changes and sacrifices to meet the demanding needs of this devastating illness. Some family carers take time from work, change or miss social events, and make personal sacrifices for their loved ones. As a patient progresses through each stage of the disease, the physical and psychological trauma is felt by the patient with heart failure but equally so by the family carer. Effective treatment options combined with the right plan improve the quality of life for both patients and family carers. A caregiver gives his account of what life is like as family living with heart failure.

Family Carer Experience:

Caregiver Experience Aged 52: Our lives were essentially flipped upside down. It was difficult to hear that our son's heart was failing and there was nothing we could do about it. Little did we know; the most difficult times were ahead. Heart failure was to become a family disease. As a family it was important to understand what heart failure was, the symptoms associated with it, the potential treatments, outcomes and how we could live a new normal. There were periods where different family members had to take time off work, adjust daily schedules and even cancel family trips. We were in this together. Although self-management for our son was important, we still were cognisant of the meals we cooked, the places we went, and the activities we participated in. Something as simple as walking a trail could be the most difficult thing in the world for a patient living with heart failure. All that to say, as family carers it was imperative to maintain our quality of life for both our mental and physical health. As with many patients, we find new ways to lead 'normal' lives, often slowing down or doing things a little differently.

4. Experiences with Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

As long as patients have access to qualified care providers with an understanding of the latest developments in heart failure treatments, most often identified by the Canadian Cardiovascular Society and Canadian Heart Failure Society guidelines adopted across the country, then placing patients on optimal therapy is a matter of following the guidelines. That being said, there is often a challenge with access to medications. Recommendations for therapies, such in the case of SGLT-II inhibitors, can be made years in advance of actual approval for use. For heart failure patients, years, months and even days on proven therapies can be the difference between a good quality of life, hospitalization, and death.

Current treatments include the 'Triple Therapy' of ACE-Inhibitors (or ARBs if ACE-I are intolerant), Beta Blockers, and MRAs. The efficacy of this triple therapy has been well established and extremely successful in managing patients' conditions with respect to reducing mortality and hospitalizations. All patients interviewed have benefited from this triple therapy. Additional treatments may include diuretics and anticoagulants. While the efficacy of current treatments is good, many patients remain intolerant to Beta Blockers and in some cases to ACE-Inhibitors, so there is a significant need to have medications to add to these patient's regimen or to even switch them to new innovative therapies. For those individuals, there is a significant need to add medications like Dapagliflozin to continue to improve patient end points for both quantity and quality of life.

We believe it is important that Dapagliflozin be accessible as soon as possible to heart failure patients who could potentially benefit from this treatment. That is why we are asking for a positive decision with respect to the submission to approve Dapagliflozin for Heart failure patients with reduced ejection fraction.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

When considering and evaluating new therapies patients and caregivers examine both quantitative and qualitative outcomes. Heart failure is the leading cause of hospitalisation for those over the age of 65 and represents a significant clinical and economic burden (Azad, N., & Lemay, G. 2014). Hospital visits due to heart failure have gone up every year for the past several years, with 60,000 reported in 2013–2014 according to the Canadian Institute for Health Information. In Canada, heart disease is the second leading cause of death after cancer, and a leading cause of hospitalization.

Qualitatively, patients and carers consider quality of life indicators and experiences such as but not limited to: spending time with loved ones, the ability to go to work on regular basis, pursuing outdoor activities, and the ability to travel. Often, and in the case of our members, quality of life takes precedent over quantity of life. Reduced hospital admissions increase quality of life indicators. John McMurray, MD, University of Glasgow, Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences said: "The benefits of dapagliflozin in DAPA-HF are very impressive, with a substantial reduction in the primary composite outcome of cardiovascular death or hospital admission. We hope these exciting new findings will ultimately help reduce the terrible burden of disease caused by heart failure and help improve outcomes for our patients."

Below is an excerpt from our patient interview exhibiting the benefits of a new therapies.

Patient Experience Aged 56: *Sure enough, at my cardiologist appointment the following week, back on the list for an ablation. May 2016 saw a failed ablation attempt, a medication change, dosage update, and a feeling that this was how I was going to live. In heart failure, with little energy. I had been on Ramipril and bisoprolol now for a while and I was convinced that my body was not liking the combination. I attended two conferences where the doctors were talking about this "miracle" drug, that they were seeing such positive results with people with heart failure. I listened, I wrote notes, I looked it up myself. I asked my cardiologist about it. I wanted a change, I argued for a change, I asked why could I not get a change. After all the testing was done again, and my doctor told me that my ejection fraction was up and I was no longer in active heart failure and I should be glad of that and not want to fix what isn't broken, I said "BUT it is broken, I feel like horrible." I am winded doing nothing but going upstairs, I sweat profusely sometimes having to change my clothes in the middle of the day, and I am tired all the time! I backed up my arguments with statistics and anecdotal evidence. In the end, he agreed to let me try it. I stopped my old medication and started the new one. Honestly, by day two, I felt better. Less winded, less sweaty, no shortness of breath. I am still feeling better, much better, physically, psychologically and soulfully even in this time of medical crisis.*

6. Experience with Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

All patient interviewees, workshop attendees, and respondents to the survey had no experience with new drug. However, when discussed, a majority of individuals were keen to understand Dapagliflozin as an addition to their current therapies and how it would benefit their quality of life.

As an organization we reviewed the results of the DAPA-HF trial, peer reviewed articles, and the recommendations from the Canadian Cardiovascular Society. The results and associated recommendations from the DAPA-HF trial are integral to our submission. The DAPA-HF trial showed dapagliflozin, when added to standard therapy reduced the risk of worsening heart failure and cardiovascular death, the absolute risk of rehospitalization, and improved symptoms of heart failure in patients with HF_{rEF} (John McMurray, University of Glasgow).

The Canadian Cardiovascular Society (CCS) heart failure guidelines program provides guidance to clinicians, policy makers, and health systems as to the evidence supporting existing and emerging management of patients with HF. In 2017 the CCS recommended the use of SGLT2 inhibitors for prevention of HF events in patients with type 2 diabetes and known history of cardiovascular disease. (CCS Society Guidelines | Volume 33, Issue 11, P1342-1433,). The CCS has since updated that recommendation with the following: We recommend SGLT2 inhibitors, such as dapagliflozin be used in patients with mild to moderate HF due to reduced LVEF ($\leq 40\%$) and without concomitant diabetes, to improve symptoms and quality of life and to reduce the risk of hospitalization and cardiovascular mortality. (Society Guidelines | Volume 36, Issue 2, P159-169, February 01, 2020).

As indicated above, guidelines suggest that dapagliflozin be added to heart patient treatment plans. Guidelines from CCS are generally adopted by the Canadian Heart Failure Society and implemented by its members across Canada. It is expected that dapagliflozin will streamline heart failure care given its ease of use and the ability to monitor patients taking the medication remotely. This is especially important during this time as current therapies present challenges such requiring lab test, blood work, titration and in person clinic visits. The heart failure population in Canada can benefit from dapagliflozin with improved clinical outcomes and improved quality of life indicators.

The decision to approve dapagliflozin is paramount in reducing the burden of heart failure for patients, healthcare professionals and Canada as a whole.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, 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.
 - a. Nothing to declare. This submission was developed and prepared solely by The HeartLife Foundation.

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.
 - a. The survey was jointly distributed by The HeartLife Foundation and The Cardiac Health Foundation of Canada.

1. 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.

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 Canada Inc.			x	
Boehringer Ingelheim Canada				x
Medtronic Canada				x
Servier Canada			x	
Novartis Canada			x	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Marc Bains
 Position: Co-Founder
 Patient Group: The HeartLife Foundation
 Date: April 18, 2020

References:

Azad, N., & Lemay, G. (2014). Management of chronic heart failure in the older population. *Journal of Geriatric Cardiology: JGC*, 11(4), 329-37

Statistics Canada. Table 102-0561 – The ten leading causes of death, 2012. CANSIM (death database) [Internet]. Ottawa (ON): Statistics Canada; 2015 Dec 10 [cited 2016 Sep 14]. Available from: www.statcan.gc.ca/pub/82-625-x/2015001/article/14296-eng.htm

Canadian Institute for Health Information. Inpatient Hospitalizations, Surgeries and Childbirth indicators in 2013–2014 [Internet]. Ottawa (ON): Canadian Institute for Health Information; 2015 Mar 5 [cited 2016 Sep 14]. Available from: <https://secure.cihi.ca/estore/productFamily.htm?locale=en&pf=PFC2805&media=0>

Heart & Stroke Foundation. (2016). *2016 Heart and Stroke Foundation Report on the Health of Canadians*. Ottawa, ON.

John Murray, University of Glasgow DAPA-HF - https://professional.heart.org/idc/groups/ahamah-public/@wcm/@sop/@scon/documents/downloadable/ucm_505122.pdf

Canadian Cardiovascular Society - Society Guidelines | Volume 33, Issue 11, P1342-1433

Canadian Cardiovascular Society - Society Guidelines | Volume 36, Issue 2, P159-169, February 01, 2020