



Common Drug Review *Patient Group Input Submissions*

dapagliflozin (Forxiga) for diabetes mellitus (Type 2)

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.

Canadian Diabetes Association — permission granted to post.

CADTH received patient group input for this review on or before May 22, 2015.

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.

While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

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Canadian Diabetes Association

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Forxiga (dapagliflozin) Type 2 diabetes
Name of patient group	Canadian Diabetes Association
Name of primary contact for this submission:	██████████
Position or title with patient group	████████████████████
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1.1 Submitting Organization

The Canadian Diabetes Association (the CDA) leads the fight against diabetes by helping people with diabetes live healthy lives while we work to find a cure. It has a heritage of excellence and leadership, and its co-founder, Dr. Charles Best, along with Dr. Frederick Banting, is credited with the co-discovery of insulin. The CDA is supported in its efforts by a community-based network of volunteers, employees, health care professionals, researchers, and partners. By providing education and services, advocating on behalf of people with diabetes, supporting research, and translating research into practical applications, the CDA is delivering on its mission.

1.2 Conflict of Interest Declarations

The Canadian Diabetes Association (the CDA) solicits and receives unrestricted educational grants from multiple manufacturers/vendors of pharmaceuticals, supplies and devices for diabetes and its complications. These funds help the CDA to support community programs and services for people with diabetes, fund research and advocacy, across Canada. Sponsors were not involved in developing this submission. The CDA did not have any conflicts of interest in the preparation of this submission.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The Canadian Diabetes Association (the CDA) solicited patient input through surveys distributed through social media and email blasts. Content of this submission is derived from 2 surveys. The first survey, conducted during 2 weeks in August 2014, gathered information from 376 Canadians with type 2

diabetes and their caregivers about the impacts of diabetes, and aspects of diabetes they want medications to address. The second survey, conducted in April 2015 during 3 weeks, provided information from Canadians with type 2 diabetes (n=349) and their caregivers (n=75) about current drug therapies and experience with Forxiga, and aspects of diabetes they would like medications to address.

2.2 Impact of Condition on Patients

Type 2 diabetes is a chronic (progressive) condition that occurs when the pancreas does not produce enough insulin or when the body does not effectively use the insulin that is produced. Insulin is a hormone that controls the amount of glucose in the blood. Common symptoms of diabetes include fatigue, thirst and weight change. High blood glucose levels can cause long-term complications such as blindness, heart disease, kidney problems, nerve damage and erectile dysfunction. The goal of diabetes management is to keep glucose levels within the target range to minimize symptoms and avoid or delay the complications.

Diabetes requires considerable self-management, including healthy eating, regular physical activity, healthy body weight, taking diabetes medications (oral and/or injection) as prescribed, monitoring blood glucose and stress management. Poor glucose control can result in serious long-term complications.

Surveyed patients were asked which aspects of diabetes were the most important. The majority of patients indicated that daily fluctuations in blood sugar were the most important aspect of diabetes to control during the day and overnight. The fluctuations impact the ability to work, interactions with friends and family, causes stress and worry as well as ability to participate in normal activities of daily living. Uncontrolled diabetes and the stigma associated with the disease can result in reduced quality of life. Maintaining control of diabetes has potential to reduce anxiety and avoid or delay complications as well as improve overall quality of life.

There was a frequent emphasis on the psychological and emotional impact of diabetes on the lives of respondents (effect on stress, anxiety, adjusting to changes in diet and lifestyle, medication and treatment management as well as relationships with family). Respondents also described fatigue, and lack of energy.

“Having diabetes makes me useless. I have no energy or strength to enjoy life anymore. I can't do partial jobs around house. I can't enjoy sports anymore. Diabetes has instill (sic) a fear in me.”

Management of diabetes includes lifestyle changes (diet, exercise and stress management). Inevitably, most patients are prescribed one or more medications to achieve glucose control. This usually starts with metformin (oral agent) and, if target glucose levels are not met, other medications are added. Over time most patients will be treated with multiple diabetes medications in order to achieve glycemic control.

Selected quotes from respondents when asked about challenges related to diabetes:

“It is a life altering disease that impacts every aspect of life. There is constant blood monitoring, diet, level of activity, cost of expensive supplies and medication.”

“The most distressing side effect of all of the diabetes drugs is they make you gain weight or prevent weight loss. It is annoying to be told to lose weight then handed a drug that prevents weight loss”

“Basically it's an awful experience, experience highs and lows. Exercising can make my sugars low so I have to always have a snack with me. Eating anywhere besides home is a challenge as you don't know how things are made. I'm constantly checking my blood and I take 13 pills a day.”

2.3 Patients' Experiences With Current Therapy

A large proportion of people with type 2 diabetes fail to achieve optimal glycemic control, which places patients at risk for both acute and chronic diabetes complications. Initial therapy is most often with metformin, but over time, most patients will require the addition of a second or third agent to reach glycemic targets. Many of the currently available second-line therapies cause significant weight gain while their ability to achieve optimal glycemic control may be limited by hypoglycemia.

A total of 397 Canadians with diabetes and caregivers indicated experience taking diabetes medications. The majority of respondents - 63% (218 people) stated they were satisfied or very satisfied with their **current therapies** whereas 18% indicated dissatisfaction. Respondents indicated current therapies resulted in better or much better blood glucose and A1C levels. However, a significant number of respondents have *not* found it easier to avoid low blood sugar (“the same,” “worse” or “much worse” for 38%), weight gain (“the same,” “worse” or “much worse” for 52%), GI effects (“the same,” “worse” or “much worse” for 57%); 59% and 55% indicating “same,” “worse” or “much worse” for dehydration and urinary tract/yeast infection, respectively.

Overall, respondents were more satisfied than dissatisfied with their medications in terms of the ability to manage their blood sugar levels. However, there were considerable issues with side effects.

Surveyed patients were also asked to rate the **importance of benefits/side effects when choosing diabetes medications**, using a five-point scale from “not at all important” to “very important.”

Over 90% of respondents indicated the following benefits of therapy were “quite” or “very important”:

- blood sugars kept at satisfactory levels in the morning/after fasting (96%),
- blood sugars kept at satisfactory levels during the day/after meals (95%),
- avoiding low blood sugar during the day/overnight (90%).

The following aspects are also considered important by the vast majority:

- avoiding weight gain (89%),
- avoiding GI effects (84%),
- reducing high blood pressure (83%),
- avoiding fluid retention (82%),
- avoiding urinary tract infection (81%).

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

The Canadian Diabetes Association (the CDA) solicited patient input on the drug being review, through a survey distributed through social media and email blasts. Conducted in April 2015 during 3 weeks, the survey provides information from Canadians with type 2 diabetes (n=349) and their caregivers (n=75) about current drug therapies and experience with Forxiga specifically, and the most important aspects of diabetes they would like new medications to address.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

The availability of dapagliflozin to offer an alternative treatment option for stabilizing blood glucose is important to patients. Dapagliflozin belongs to a new class of drugs to lower blood glucose through inhibition of subtype 2 sodium-glucose transport protein (SGLT2), which is responsible for at least 90% of the glucose reabsorption in the kidney. The SGLT2 inhibition also causes a reduction in blood pressure and weight loss.

A total of 92 respondents indicated they (or people with diabetes for whom they care) are taking Forxiga now, and 6 had to stop for reasons other than completion of a clinical trials; 47 have taken other drugs in the same class i.e. Invokana (canagliflozin) or Jardiance (empagliflozin). Patients and caregivers who have experience with Forxiga, highlighted its effectiveness in **lowering blood sugar and blood pressure** compared to other medications. The improvement in blood sugar levels (“fasting and throughout the day”) and the accompanying weight loss – described as “significant” and “dramatic” -- was observed among many who had struggled with keeping glucose at target: “his blood sugar are below 10, he hasn't been below 10 in years, the other day, it was 6.3 that's amazing;” “Readings are best I have ever had;” “bloods sugars the best they have been since diagnosis a year ago.” Many who have only been on the medication for a short period of time noticed instant improvement: “I have only taken it for four days and I already feel the effects, which are positive!!” “I've only been on Forxiga for a month, but seems to be doing the job where the other was not quite working.” Many respondents noted less dependency on other drugs such as insulin as a result of Forxiga -- one person was able to get off “one of 3 blood pressure meds,” while another “reduced insulin intake by 75%.” The reduction of medications is viewed as a substantial improvement to quality of life: “Forxiga has replaced two of my insulin needles (breakfast and lunch). Not having to give myself two less needles a day has improved my life drastically.” In addition, respondents generally did not describe serious side effects; some who did experience side effects such as frequent urination, dehydration, increased appetite described them as “manageable.”

Below are other quotes from patients/caregivers who have found the experience with Forxiga very positive, including its effects on their **energy level** and **mental health**:

“I have only been taking it for a month but it has helped me feel more in control of my diet thus helping me eat better and exercise more.”

“I have lost a surprising amount of weight in a short time. This helps me remain optimistic about my health improving significantly in the long run.”

“Absolute game changer!!! My numbers were up in the high teens...now numbers are normal, I'm not constantly thirsty[sic] or urinating, my weight has dropped and I feel great! This weight loss has helped put me in a very positive frame of mind and has helped me get off my Anti Depression drugs also.”

“I have been of Forxiga only three weeks, but I have lost 7 lbs, my sugars are getting better and I feel less tired. I feel more like my old self.”

“for me it is the best thing ever with my combination of meds. it is working for me first time my body has been happy i can not tell you how good my body feels”

“Huge benefit in reducing fasting glucose and HbA1c. Significant weight reduction (loss of > 4 Kg) evident in first 3 months. Very +ve impact on my self-confidence and feeling of "being in control" with my diabetes.”

While most respondents had positive experience with the medication, some have not experienced the same benefits and have found side effects challenging – two respondents had to discontinue the medication because of “face... swollen and broke out in a rash” and “concerns about bladder cancer”:

“I’ve been on it two months now, and it seems as if it takes a long time for results to show. Though I have lost weight and my blood pressure is more stable. My morning sugar levels are still higher than I’d like.”

“I started taking it about one month ago. I was prescribed 5 mg once daily. My test results did not show improvement and I did not lose weight. My doctor changed my prescription to 10 mg daily. It’s only been a couple of days and I don’t feel any differences at this point.”

“First week experienced vaginal yeast infection, severe constipation and a small weight loss. Subsequently no side effects, no weight loss and no significant change in blood sugar levels.”

“I’ve used forxiga for 2 months and I am now feeling the effects, mineable constipation and I am adjusting my insulin greatly I now use about half the insulin and I still have lows during the day. My physical activity has increased but unfortunately the weight lose[sic] has not happened yet, still hoping.

“Did low blood sugar levels but did not reduce weight. Caused repetitive yeast infections and urinary tract infections as well as unpredictable bouts of bowel incontinence. I have never felt so ill in my life.”

“have only been taking Forxiga for 2 months... but seems to be increasing my blood Pressure and I have also developed [an] annoying pang in my chest.”

“Vaginal yeast infections that I had one after another and constant chapped lips that burned and split were part of the side effects.”

How important is the access to Forxiga (dapagliflozin)?

Over 90% of respondents who have had experience of Forxiga (**dapagliflozin**) indicated that its availability is “important” or “very important” to people living with type 2 diabetes (n=84 out of 93 responses). Among respondents who have taken diabetes medications, 70% indicated it is important for Forxiga to be available (n=225 out of 321 responses). The reasons cited included aforementioned benefits such stabilizing blood glucose levels, weight loss and minimal side effects as compared to other medications. Some emphasized the importance of giving patients options particularly if other medications don’t work:

“Everyone should be given the opportunity to test new medications to determine whether it is the best treatment for them.”

“[Forxiga has]... changed my life. They have exceeded my expectations in terms of helping me manage my Diabetes. New Medications like these should be covered so other Canadians can benefit like I have and reduce the risk of CV events and the cost of these events to our Health Care system.”

As some respondents were offered Forxiga as part of a clinical trial or “free of charge by the manufacturer”, they worried about not being able to afford it after the trial ended.

In summary, diabetes requires intensive self-management and can be challenging; as one respondent put it: “Managing diabetes is very stressful because you take lots of medication and in spite of your best efforts, maintaining target ranges is difficult.” To achieve optimal blood glucose levels, individualization of therapy is essential, including selecting the drug or combination of drugs, route of administration (oral, injection, pen or pump), how frequently the patient monitors blood glucose and adjusts dosage, the benefits and risks that the patient experiences and/or tolerates, and the lifestyle changes the patient is willing or able to make.

Patient Group Input Submissions

There are clear expectations that new drugs should offer better blood glucose control to prevent hyperglycemic and hypoglycemic episodes, as well as longer term control, with minimal side effects and long term damage to organs, at affordable costs, and reduced dependency on other drugs such as insulin. Based the experience of respondents, many of these expectations were met by dapagliflozin in providing better control of blood glucose levels and of diabetes in general.

Some people did not have a positive experience, which reinforces the understanding that different people living with diabetes require different options in terms of medications to help effectively manage their disease. Their clinical profile, preference and tolerance of therapy can direct physicians to the most appropriate drug therapy. The availability of Forxiga (dapagliflozin) thus provides an important option for patients.

Appendix: Organizations and foundations that made donations to the Canadian Diabetes Association between September 2012 and August 2013. (Source: CDA 2013 Annual Report)

593123 Alberta Ltd.	Chartwell Retirement Residences	Guelph Community Foundation	MedicAlert	Saskatchewan Indian Gaming Authority	The Lorne & Evelyn Johnson Foundation
A. Lassonde Inc.	Children's Hospital Aid Society	Home Hardware Stores Ltd.	Medisys Health Group	Saskatoon Community Foundation	The North West Company Inc.
Abbott Laboratories, Ltd.	Chippendale Foundation	Honeybush Health Ltd.	Medtronic of Canada Ltd.	Saskatoon Subway	The Poker For Diabetes Foundation
Aecon Group Inc.	CIBC	HOPE Ottawa Carleton Inc.	Merck Canada	Shaw Communications Inc.	The Toronto Star Fresh Air Fund
Affinity Credit Union	Clifford & Lily Fielding Foundation	Husky Energy Inc.	MLF Consulting Ltd.	Shopesse Foods Inc.	The Toronto-Dominion Bank
Agway Metals Inc.	CMG Computer Modelling Group Ltd.	Information Services Corporation (ISC)	National Bank of Canada	Silver Hills Bakery	The Winnipeg Foundation
Amgen Canada Inc.	Community Foundation of Ottawa	Janssen Inc.	Nestlé Health Science	South Saskatchewan Community Foundation Inc.	TransCanada Pipelines Ltd.
Amor Da Patria Community Centre of Toronto	Community Initiatives Fund	Janzen's Pharmacy Ltd.	Newfound Foundation	Stickling's Specialty Bakery Ltd.	Unilever Canada Inc.
Animas Canada	Compass Pharmacies	Jarrold Oils Ltd.	Novartis Pharmaceuticals Canada Inc.	Storck Canada Inc.	Union 52 Benevolent Society
AstraZeneca Canada Inc.	Conexus Credit Union	Jewish Foundation of Manitoba	Novo Nordisk Canada Inc.	Strategic Charitable Giving Foundation	United Way Newfoundland & Labrador
Balmoral Office Group Inc.	Co-operators/CUMIS	John Ung-Ling Ting Professional Corporation	Order Of The Eastern Star – Grand Chapter of NS & PEI	Subway Franchisee Advertising	Wellington Laboratories Inc.
Bayer HealthCare – Diabetes Care Division	Covidien Canada	John Zubick Ltd.	Pacific Blue Cross Health Foundation	Sudbury Rocks Running Club	Williamsburg Arms
Bayshore Home Health	Dauphin Clinic Pharmacy	Johnson & Johnson Inc.	Performance Boat Club Charities	Sun Life Financial	
BD Medical – Diabetes Care	Donors Choice – Killarney & Area	Kiwanis Club of Vancouver	Pfizer Canada Inc.	Sunrise Soya Foods	
BHP Billiton Matched Giving Program	E-L Financial Corporation Ltd.	KPMG	Pharmasave Central	Sure Flow Equipment Inc.	
Blistex Corporation	Eli Lilly Canada Inc.	Kraft Canada Inc.	Progressive Foods Inc.	Takeda Canada Inc.	
Boehringer Ingelheim (Canada) Ltd.	Eli Lilly Canada Inc./Boehringer	Lagniappe Foundation	Project Read Literacy Network	TD Waterhouse	
Brian & Susan Thomas Foundation	Excelleris Technologies LP	Lawson Foundation	Raymond James Canada Foundation	TELUS	
Bristol-Myers Squibb/AstraZeneca Canada Alliance	Flame Of Hope Golf Classic London	Leon's Furniture Ltd.	RBC Foundation	The Arthur J E Child Foundation	
Cal LeGrow Foundation	General Mills Canada Corporation	LifeScan Canada Ltd.	Realty Executives Western Canada	The Calgary Foundation	
Cal Wenzel Family Foundation	Genzyme Canada Inc.	Lions Clubs of Canada	Rexall Foundation	The Cash Store Financial Services Inc.	
Cameco Corporation	GlaxoSmithKline Inc.	Loblaw Companies Ltd.	Regina Capital Cosmopolitan Club	The Charles Norcliffe Baker & Thelma Scott Baker Foundation	
Canadian Footwear Ltd.	Glenn's Helping Hand Foundation Inc.	Loyal Protestant Association	Regina Queen City Kinsmen	The Chastell Foundation	
Canadian National Railway Company	Gold Bond Ultimate	Manitoba Association of Health Care Professionals	Rexall Foundation	The Community Foundation of Prince Edward Island	
Canola Info/Canola Council of Canada	Government of Canada – Province of New Brunswick	Manulife Financial	Roche Diagnostics Canada	The John & Judy Bragg Family Foundation	
Cenovus Energy – Employee Foundation	Grand Court Order of The Amaranth	Mark's Work Wearhouse	Rubicon/Pharmasave	The Kinsmen Club of Saskatoon	
Chadi & Company	Great-West Life, London Life & Canada Life	Masonic Foundation of Ontario	Rx&D, Canada's Research-Based Pharmaceutical Companies	The London & District Concrete Forming Contractors Assoc.	
	Green Shield Canada	Masons	Sandra & Leo Kolber Foundation		
		McNeil Consumer Healthcare	Sanofi Aventis Canada Inc.		
		Medavie Health Foundation			
		MEDEC			