



Common Drug Review *Patient Group Input Submissions*

Jardiance (empagliflozin) Type 2 diabetes

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 14, 2015

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Canadian Diabetes Association

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Jardiance (empagliflozin) Type 2 diabetes
Name of the patient group	Canadian Diabetes Association
Name of the primary contact for this submission:	██████████
Position or title with patient group	████████████████████
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Permission is granted to post this submission	Yes

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, provides information from Canadians with type 2 diabetes (n=349) and their caregivers (n=75) about current drug therapies and experience with Jardiance (empagliflozin), and the most important 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:

“Managing diabetes is very stressful because you take lots of medication and in spite of your best efforts, maintaining target range is difficult.”

“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.”

“...problems are mostly trying to lose weight....Took 5 Metformin pills (1 a day for 5 days) and put on 2 pounds a day. Took over a month to lose that 10 pounds.”

“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. They indicated they were better or much better at keeping blood glucose and A1C levels at target. 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 following 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 “quite important” or “very important” regarding the following benefits of therapy:

- 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%).

Some respondents simply wanted drugs to “allow them to lead as normal a life as possible” and provide a “life without concerns about complications because of diabetes.”

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 reviewed, 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 empagliflozin 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 empagliflozin to offer an alternative treatment option for stabilizing blood glucose is important to patients. Empagliflozin 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.

Given that empagliflozin is not currently available on the Canadian market, only 14 respondents indicated they have either taken empagliflozin in past clinical trial or are taking it now as part of a clinical trial; 136 have taken other drugs in the same class i.e. Invokana (canagliflozin) or Forxiga (dapagliflozin). Patients who have taken empagliflozin noted its effectiveness in keeping blood sugar levels at target and decreasing side effects (diarrhea, stomach ache, losing weight), and provide “better quality of life” from their perspective. A patient who has used empagliflozin in a past trial and now on another class of drugs expressed his wish that empagliflozin would be “approved” in Canada because “it worked...[other drugs] cause weight gain and do not work as well as empagliflozin.”

For people who have *not* had experience with empagliflozin, they have indicated the following as important aspects to address with new drugs:

- Maintain blood glucose levels & reduce instances of hypoglycemia (“managing levels becomes less stressful”)
- Better A1C
- Minimal side effects (“without increasing risk of renal damage”)
- Slow the progression of disease/complications (“reduce vascular risks”, “reduce number of patients on dialysis, losing limbs, heart problems, organ failures”)
- Better blood pressure
- Reduction of other diabetes meds
- Avoid or delay insulin
- Weight loss/no weight gain
- Lower cost/fully covered under public drug plans (“for retired persons with limited budgets”)
- Cure the disease
- Combat depression (“If these meds can help you feel better it will help with the depression of Diabetes. It may reduce the fear of future serious complications.”)

In general, all patients hope to have blood glucose levels, avoid hypoglycemia, avoid long term complications and live a healthy life. A large number of respondents also hope to reduce the number of drugs taken, as well as insulin injections. One respondent stated: “if medications can help reduce the amounts or frequency of injections without the risk of serious side effects I would welcome that.” Another respondent puts it in perspective: “I hope one day to be able to take only one or two medications to control my diabetes rather than the 3 injectables and 2 tablet medications I take now.” Other respondents would like the new drug to help “reduce the number [and] types of pills that a type 2 diabetic takes,” “keep away from the needle,” “reduce/eliminate/replace the need for insulin.” Ultimately, people with type 2 diabetes hope for the least number of meds possible at an affordable cost: “I hope that it would be a one tablet or injection instead of multiple medications to treat type 2

diabetes and that everyone can afford to use it.” A great number of patients also expressed their hope for a cure.

How important is the access to empagliflozin?

Over 66% of respondents who have taken empagliflozin indicated that its availability is important to people living with type 2 diabetes. Among respondents who are on diabetes medications, 57% (n=179 out of 316) indicated it is important for empagliflozin to be available. While most of these respondents have not had direct experience with empagliflozin, they indicated the importance to provide alternatives and options to patients:

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

“[drugs that have] the potential to lower weight/reduce weight gain and blood pressure while keeping BG at target in some people with diabetes...should be made available and affordable.”

Some patients reinforced their hope for a new drug to eliminate the need to take multiple drugs (“If I can take one medication rather than 3 and still be well controlled, there should be less cost and side effects”) and the wish to learn more about side effects such as potential renal damage.

In summary, diabetes requires intensive self-management. 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.

There are clear expectations that any new drugs should offer good 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, and at affordable costs. Many patients also hope that new medications can help reduce the number and types of drugs taken including insulin injections. The patients who had experience with empagliflozin described good results in terms of glucose control and less side effects such as weight gain/GI effects.

Responses to this survey reinforce 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. As noted by a respondent: **“open access to this new class of diabetes therapy [would allow] physicians and patients [to] have the flexibility to find the most effective and safe "mix" of drugs to maintain control of diabetes. Diabetes changes over time, and everyone needs different medications at different times of their life with diabetes.”** The availability of the Jardiance (empagliflozin) provides an important option for patients.

Appendix 1: 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
A. Lassonde Inc.	Children's Hospital Aid Society	Home Hardware Stores Ltd.	Medisys Health Group	Saskatoon Community Foundation
Abbott Laboratories, Ltd.	Chippendale Foundation	Honeybush Health Ltd.	Medtronic of Canada Ltd.	Saskatoon Subway
Aecon Group Inc.	CIBC	HOPE Ottawa Carleton Inc.	Merck Canada	Shaw Communications Inc.
Affinity Credit Union	Clifford & Lily Fielding Foundation	Husky Energy Inc.	MLF Consulting Ltd.	Shopease Foods Inc.
Agway Metals Inc.	CMG Computer Modelling Group Ltd.	Information Services Corporation (ISC)	National Bank of Canada	Silver Hills Bakery
Amgen Canada Inc.	Community Foundation of Ottawa	Janssen Inc.	Nestlé Health Science	South Saskatchewan Community Foundation Inc.
Amor Da Patria Community Centre of Toronto	Community Initiatives Fund	Janzen's Pharmacy Ltd.	Newfound Foundation	Stickling's Specialty Bakery Ltd.
Animas Canada	Compass Pharmacies	Jarrold Oils Ltd.	Novartis Pharmaceuticals Canada Inc.	Storck Canada Inc.
AstraZeneca Canada Inc.	Conexus Credit Union	Jewish Foundation of Manitoba	Novo Nordisk Canada Inc.	Strategic Charitable Giving Foundation
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
Bayer HealthCare – Diabetes Care Division	Covidien Canada	John Zubick Ltd.	Pacific Blue Cross Health Foundation	Sudbury Rocks Running Club
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 Ingelheim Alliance	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 Alliances	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	Regina Capital Cosmopolitan Club	The Cash Store Financial Services Inc.
Cameco Corporation	GlaxoSmithKline Inc.	Loblaw Companies Ltd.	Regina Queen City Kinsmen	The Charles Norcliffe Baker & Thelma Scott Baker Foundation
Canadian Footwear Ltd.	Glenn's Helping Hand Foundation Inc.	Loyal Protestant Association	Rexall Foundation	The Chastell Foundation
Canadian National Railway Company	Gold Bond Ultimate	Manitoba Association of Health Care Professionals	Roche Diagnostics Canada	The Community Foundation of Prince Edward Island
Canola Info/Canola Council of Canada	Government of Canada – Province of New Brunswick	Manulife Financial	Rubicon/Pharmasave	The John & Judy Bragg Family Foundation
Cenovus Energy – Employee Foundation	Grand Court Order of The Amaranth	Mark's Work Wearhouse	Rx&D, Canada's Research-Based Pharmaceutical Companies	The Kinsmen Club of Saskatoon
Chadi & Company	Great-West Life, London Life & Canada Life	Masonic Foundation of Ontario	Sandra & Leo Kolber Foundation	The London & District Concrete Forming Contractors Assoc.
	Green Shield Canada	Masons	Sanofi Aventis Canada Inc.	
		McNeil Consumer Healthcare		
		Medavie Health Foundation		
		MEDEC		