



Common Drug Review *Patient Group Input Submissions*

empagliflozin and metformin (Synjardy) 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 24, 2016.

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

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Canadian Diabetes Association

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Synjardy (empagliflozin and metformin) Type 2 diabetes
Name of the patient group	Canadian Diabetes Association
Name of the primary contact for this submission:	[REDACTED]
Position or title with patient group	[REDACTED]
Email	[REDACTED]
Telephone number(s)	[REDACTED]
Name of author (if different)	[REDACTED]
Patient group's contact information:	
Email	Canadian Diabetes Association
Telephone	advocacy@diabetes.ca
Address	613 688 5938
Website	http://www.ctac.ca
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 three surveys. Two surveys conducted in August 2014 and October 2015, gathered information Canadians with type 2 diabetes and their caregivers about the impacts of diabetes, and aspects of diabetes they want medications to address; the surveys were answered by 376 and 212 individuals, respectively. The third 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. Common symptoms of diabetes include fatigue, thirst and weight change. 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 complications, such as heart disease, stroke, blindness, 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.

Direct quotes below describe the general impact of diabetes on respondents:

“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.”

“I need to be careful with what I eat and how much I eat, especially carbohydrates. Also need to balance out a snack, insulin needs and exercise to ensure I don't have a hypoglycemic episode while exercising. I also need to monitor my insulin needs while doing errands, again to avoid a hypoglycemic episode.”

“[Diabetes has] affected my family also due to my being not able to work while I was waiting for a kidney transplant, which was given to me by ... my son. Because of being on dialysis [sic] I had to spend most of my life's savings. Being sick can be very very expensive.”

“It is difficult to lead a normal life when you always need to be taking meds or checking your [blood sugar] levels and reading labels on all your food while your [blood sugar] levels change with or without food intake. The impact of diabetes on all your other organs is another huge problem and when you treat one you harm another. Most difficult disease to manage.”

Many respondents described fatigue and lack of energy. There was also 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). Below are selected quotes that demonstrate challenges due to diabetes:

“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.”

“...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 loose[sic] 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.”

Surveyed patients were asked which aspects of diabetes were the most important. The majority of patients indicated that daily fluctuations in blood sugar and weight gain were the most important aspects of diabetes to control. The blood sugar 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. Weight gain 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.

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. The initial therapy is most often 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 therapies cause significant weight gain while their ability to achieve optimal glycemic control may be limited by hypoglycemia. Weight gain adds to the sense of failure and anxiety in this patient population who frequently blame themselves for their health status.

In our April 2015 survey, a total of 377 Canadians with type 2 diabetes and caregivers for those with diabetes indicated experience taking diabetes medications. The medications taken by respondents at the time of survey included metformin (173), insulin (121), sulfonylureas (73), DPP-4 inhibitors (43), SGLT2 inhibitors (120), GLP-1 agonists (26), DPP-4 inhibitors (43), combinations of DPP-4 inhibitors and metformin (62), meglitinides (13), TZDs (8), rosiglitazone+metformin (8), and acarbose (4). Some people indicated that they had had to stop the following medications for reasons other than the end of clinical trials: metformin (26), sulfonylurea (42), SGLT2 inhibitors (15), DPP-4 inhibitors (20), DPP-4 inhibitors and metformin combination (14), meglitinides (4), TZDs (38), rosiglitazone+metformin (8), GLP-1 agonists (2), acarbose (2), and insulin (8).

Among the 173 people who were on metformin at time of survey, a large proportion were taking additional medications to manage their diabetes: 49 were also taking a sulfonylurea, 72 were taking a SGLT2 inhibitor, 32 were taking a DPP-4 inhibitor, 11 were taking a combination drug of DPP-4 inhibitor and metformin, 19 were taking a GLP-1 agonist, 7 using meglitinides, 2 on acarbose, 3 using TZDs, 3 using combined rosiglitazone+metformin, and 70 were on insulin. These sub-groups are not mutually exclusive as some patients were taking multiple drugs.

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.

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%).

Other aspects deemed important when choosing medications include “avoiding kidney strain and heart problems” and “depression.” 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 2 — Condition and Current Therapy Information

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?

Empagliflozin belongs to a new class of drugs that 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 stabilizes blood glucose, reduces blood pressure and promotes weight loss. Recently published results of the first cardiovascular outcome trial of this drug class demonstrate lower rates of cardiovascular-related hospitalization and mortality in patients who used empagliflozin. The availability of empagliflozin offers an alternative treatment option for people with type 2 diabetes, as well as those at higher risk for cardiovascular events.

Only 14 respondents indicated they had taken empagliflozin in as part of a clinical trial; 136 had 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 minimizing side effects (e.g. diarrhea, stomach ache, weight gain), 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 he could access it 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 reported challenges with some of the current medications such as GI effects associated with metformin use, and 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
- Weight loss/no weight gain
- 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”)

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- Better blood pressure
- Reduction of other diabetes meds
- Avoid or delay insulin
- 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 under control, avoid hypoglycemia, avoid long term complications. 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 medications 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.” Given the wishes expressed by many respondents with type 2 diabetes to reduce the number of medications, the availability of Synjardy, as a fixed dose combination of metformin with empagliflozin, for people with type 2 diabetes stabilized on metformin, empagliflozin (with or without a sulfonylurea or insulin) would serve the purpose of offering effective therapy while reducing pill burden and promoting adherence to prescribed therapy. This would offer a significant advantage for doctors and patients working together to achieve optimal treatment with the lowest effective dose.

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. Given the challenge that many patients have with weight loss and the enormous sense of failure experienced with weight gain, diabetes drugs that promote weight loss can be an important part of care.

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. 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. Several respondents identified taking several medications as a concern, hoping to have access to combined medicines which would reduce the number of medications taken. The availability of a combined empagliflozin and metformin (Synjardy) may promote adherence to prescribed treatment by reducing pill burden and can offer some patients a good alternative for effective management of diabetes.

Appendix: Organizations and foundations that made donations to the Canadian Diabetes Association in 2015. Source: CDA 2015 Annual Report, available at <http://www.diabetes.ca/getmedia/0204ddb9-8942-4033-9dca-21547d2d8007/2015-cda-annual-report.pdf.aspx>

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Foundations Airlie Foundation Alice & Murray Maitland Foundation Alpha Gamma Delta Foundation Aquaduct Foundation AWB Charitable Foundation Brantford Community Foundation – City of Brantford Brian & Susan Thomas Foundation Burrows Colden Family Foundation Butler Family Foundation Cal Wenzel Family Foundation Calgary Shaw Charity Classic Foundation Cambridge & North Dumfries Community Foundation Canadian MedicAlert Foundation Cenovus Employee Foundation Chickadee Trust Chimp Foundation Colin & Lois Pritchard Foundation Community Foundation for Kingston & Area Community Foundation of Ottawa-Carleton Crabtree Foundation Deloitte Foundation Canada Edmonton Community Foundation Edwards Charitable Foundation EnCana Cares Foundation Ernst Hansch Foundation/ Terracon Development Eva T. Villanueva Charitable Fund at the Strategic Charitable Giving Foundation Flaman Foundation Fleming Foundation Fredericton Community Foundation Inc. 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