Section 1 – General Information

| Name of the drug CADTH is reviewing and indication(s) of interest | Invokana (Canagliflozin)  
Type 2 Diabetes |
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<tr>
<td>Name of patient group</td>
<td>Canadian Diabetes Association</td>
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<tr>
<td>Name of primary contact for this submission:</td>
<td>Seema Nagpal</td>
</tr>
<tr>
<td>Position or title with patient group</td>
<td>Director, Public Policy</td>
</tr>
<tr>
<td>Email</td>
<td><a href="mailto:seema.nagpal@diabetes.ca">seema.nagpal@diabetes.ca</a></td>
</tr>
<tr>
<td>Telephone number(s)</td>
<td>613 688 5938</td>
</tr>
<tr>
<td>Name of author (if different)</td>
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<tr>
<td>Patient group's contact information:</td>
<td>Canadian Diabetes Association</td>
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<tr>
<td>Email</td>
<td><a href="mailto:advocacy@diabetes.ca">advocacy@diabetes.ca</a></td>
</tr>
<tr>
<td>Telephone</td>
<td>613 688 5938</td>
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| Address | 45 Montreal Road  
Ottawa, ON, K1L 6E8 |
| Website | www.diabetes.ca |
1.1 Submitting Organization
The Canadian Diabetes Association (the Association) 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 Association 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 Association is delivering on its mission.

1.2 Conflict of Interest Declarations
The Canadian Diabetes Association (the Association) solicits and receives unrestricted educational grants from multiple manufacturers/vendors of pharmaceuticals, supplies and devices for diabetes and its complications. These funds help the Association 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 Association 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 Association) solicited patient input through a survey distributed through social media and email blasts. The survey was open for approximately 2 weeks and included questions on how diabetes impacts the lives of patients, current drug therapy, previous experience with drug therapy and experience with canagliflozin (Invokana). Among the 388 individuals who responded, 92.8% identified themselves as patients living with type 2 diabetes, 4.1% as caregivers for someone with type 2 diabetes, 0.5% as having type 1 diabetes, and 2.6% as other. The survey data reported in this submission are from those people living with diabetes or caring for someone with type 2 diabetes (n=376). Of those 376 responding 93% are taking (or had taken) diabetes medication. Approximately 7.6% (n=13) had taken canagliflozin. A total of 250 respondents completed the full questionnaire with a range from 388 to 250 respondents for individual questions.

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.

Patients in the survey 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. Many patients with diabetes do not take oral glucose-lowering therapy as prescribed. Almost 30% of respondents found it somewhat difficult, difficult, or very difficult to take multiple medications through the day. Given that diabetes frequently occurs with other chronic conditions, this finding has significant implications for the diabetes population.

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.”

“...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 that 10 pounds.”

Approximately 56% of all respondents indicated general satisfaction (satisfied or very satisfied) with drug therapy. Yet this respondent stated the greatest desire of all people living with diabetes:

“I am always wishing that there would be a PERMANENT cure for Diabetes Type 2.”

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.
Surveyed patients were asked to “rate” the importance of various benefits and risks associated with diabetes medications, using a five-point scale from “not at all important” to “very important.” The most important benefit of therapy was noted as “blood sugars kept at satisfactory levels” during the day and overnight. Respondents also acknowledged “GI side effects” and “losing or not gaining weight” as important factors in selecting their individual drug therapy. This is consistent with qualitative responses provided, for example:

“I am fighting high blood sugars. .... I exercise - walking the dog - and generally follow a healthy eating routine but still end up with morning highs. It gets very frustrating having to count carbs all the time and never being able to eat anything extra without getting a high. I take many drugs.....started a new one, but after 6 weeks of nausea my doctor took me off it.”

Respondents were asked to provide, in their own words, the benefits and side effects of their drug therapy. All responses were categorized by theme and then grouped by sub-themes. The majority respondents stated they were mostly satisfied with drug therapy and with the fact that their blood sugar levels were kept at target. However, a significant number of respondents struggled with fluctuations and expressed extreme frustration with the lack of control. Several respondents identified previous prescribed drugs as having intolerable side effects – mostly hypoglycemia, morning hyperglycemia and gastrointestinal effects, including nausea and diarrhea. Other concerns raised from respondents were related to the need for multiple medications, cost of treatment, and lack of insurance coverage.

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

Section 3 — Information about the Drug Being Reviewed

The availability of canagliflozin to offer an alternative treatment option for stabilizing blood glucose is important to patients. Canagliflozin, 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.

Respondents were asked to rate their level of knowledge of the canagliflozin (Invokana), regardless if they have taken the drug using a four-point scale from “have not heard about” to “know a lot about”. Respondents had very little knowledge of canagliflozin, with 10% of respondents indicating some knowledge and 2% indicating a lot of knowledge. Among those surveyed, the most frequent expectation for any new therapy was to have better blood glucose control, including fewer instances of hyperglycemia and hypoglycemia. While most indicated the expectation of fewer side effects (including hypoglycemia and weight gain), others indicated they worry about any side effects of medications.

Only 13 respondents had drug experience with canagliflozin. Of these, 10 people qualitatively described treatment. Four were very pleased with the glucose control and experienced no notable side effects. These patients described the relief of finally receiving treatment that controlled their blood glucose. “Just started taking Invokana, it has made a huge difference in my blood sugars. I seem to finally have the right combination.”
“I like the fact that there is little to no side effects associated with these medications.”

“It has actually lowered my blood sugar levels to a range of readings that I haven’t seen in several years.”

Three patients described increased urination, one described persistent yeast infection. One of these patients discontinued canagliflozin due to the frequent urination.

Survey respondents were asked how important is it to have new drug therapy for glucose lowering also reduce weight. Approximately 78% indicated that it was between important to essential that these drugs also reduce weight.

Survey respondents were asked how important is it to have new drug therapy for glucose lowering also reduce blood pressure. Approximately 80% indicated that it was between important to essential that these drugs also reduce blood pressure.

Approximately 80% of respondents indicated that the availability of canagliflozin is important to people living with diabetes. Patients stated:

“Weight & hypertension are often problems for diabetics & contribute to many complications of diabetes.”

“It gives Dr. more options to try for patients”

In summary, diabetes is a very common chronic progressive condition that 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 new drugs should offer better blood glucose control to prevent hyperglycemic and hypoglycemic episodes, as well as longer term control. The patients with canagliflozin experience stated good results in terms of glucose control. A few patients described increased urination and one described a yeast infection; once patient discontinued therapy after 3 weeks.

Responses to this survey reinforce the understanding that people living with diabetes often have co-morbidities including overweight/obesity, hypertension and other chronic conditions. Their clinical profile and preference and tolerance of therapy can direct physicians to the most appropriate drug therapy. The availability of the canagliflozin provides an important option for patients.
Appendix: Organizations and foundations that made donations to the Canadian Diabetes Association between September 2012 and August 2013.