CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**TBC (semaglutide),** **Diabetes mellitus, type 2**
Name of the Patient Group	**Diabetes Canada**
Author of the Submission	**Samantha Ghanem**
Name of the Primary Contact for This Submission	**Seema Nagpal**
Email	**seema.nagpal@diabetes.ca**
Telephone Number	**613-688-5938**

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.

Diabetes Canada is a national health charity representing approximately 11 million Canadians living with diabetes or prediabetes. Diabetes Canada leads the fight against diabetes by helping those affected by diabetes live healthy lives, preventing the onset and consequences of diabetes, and discovering 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. Diabetes Canada 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 living with diabetes, supporting research, and translating research into practical applications, Diabetes Canada is delivery on its mission. We will continue to change the world for those affected by diabetes through healthier communities, exceptional care, and high-impact research.

For more information, please visit: www.diabetes.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.

This submission contains patient input from online surveys conducted in November 2019, November 2018, and October 2016. The surveys were open for two weeks to people across Canada and consisted

of self-administered questionnaires. The surveys were directed at people living with type 2 diabetes and caregivers of people living with type 2 diabetes and inquired about respondents' lived experience with diabetes and diabetes medications, and expectations for new drug therapies in Canada. Further, the November 2019 and November 2018 surveys posed several questions specifically about the drug under review, semaglutide. Awareness about the surveys was generated through Diabetes Canada's social media channels (Twitter and Facebook); the October 2016 survey was also advertised to Diabetes Canada email subscribers through e-blasts.

The November 2019 survey had 20 respondents; 19 identified as living with type 2 diabetes while one identified as a caregiver to someone living with type 2 diabetes. Of the 20 respondents, eight indicated their age and date of diagnosis. The eight respondents varied in age, 62.5% were between the ages of 25 and 69 years, and 37.5% were over 70 years old. Further, of the eight respondents, 50.0% reported having lived with diabetes for 1 to 10 years and the other 50.0% reported having lived with diabetes for 11 to 20 years.

The November 2018 survey had 15 respondents; 13 respondents identified as living with type 2 diabetes while two identified as being a caregiver to someone living with type 2 diabetes. Of the 15 respondents, 6 indicated their age and date of diagnosis. Of the 6 respondents, all were over the age of 40 years, with 33.3% each in the 40-54, 55-69, and over 70-year age categories. The majority (n=4, 66.7%) reported having lived with diabetes for 6 years or more.

The October 2016 survey had 847 respondents; 790 respondents identified as living with type 2 diabetes while 57 identified as being caregivers to someone with type 2 diabetes. Of the respondents who indicated their age and date of diagnosis (n=379, 44.7%), 70.1% (n=266) were over the age of 55, with the largest number of respondents (55.7%, n=211) in the 55-69 year old category, and 60.2% (n=228) having lived with diabetes for over 10 years (17.2% of this group reported having lived with diabetes for over 20 years).

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?

Diabetes is a chronic, progressive disease with no known cure. Type 1 diabetes occurs when the body produces either little or no insulin. Type 2 diabetes occurs when the pancreas does not produce enough insulin or the body does not effectively use the insulin that is produced. Common symptoms of diabetes include extreme fatigue, unusual thirst, frequent urination, and weight change (gain or loss).

Diabetes requires considerable self-management, including eating well, engaging in regular physical activity, maintaining a healthy body weight, taking medications (oral and/or injectable) as prescribed, monitoring blood glucose, and managing stress. Poor glucose control is serious and problematic. Low blood glucose can precipitate an acute crisis, such as confusion, coma, and/or seizure that, in addition to being dangerous themselves, may also contribute to a motor vehicle, workplace, or other type of accident causing harm. High blood glucose over time can irreversibly damage blood vessels and nerves, resulting in blindness, heart disease, kidney problems, and lower limb amputations, among other issues. The goal of diabetes management is to keep glucose levels within a target range to minimize symptoms and avoid or delay complications.

Most respondents who participated in the November 2019, November 2018, and October 2016 survey spoke negatively of their experiences living with diabetes. Respondents expressed that diabetes is "manageable but a bother", "a constant battle every day", "a terrible way of life", an "emotional rollercoaster", inconvenient, frustrating, exhausting, and a constant source of worry. One respondent said it just "isn't fun to have to live with", while another commented "it has been life changing, not in a good

way.” A third responder indicated that their “whole life style has been changed.” A fourth respondent mentioned “it has definitely impacted my life and the things that I used to do, that I don't enjoy doing any longer”. Several people spoke about its permanence, emphasizing that there is no “holiday” from diabetes.

The majority of survey respondents spoke about the adverse impacts diabetes has had on their lives. They indicated that they are constantly thinking about and planning around their disease. Further, that diabetes affects their everyday activities including eating, exercising, working, and socializing. Overall, diabetes makes it difficult to be flexible and spontaneous, as it requires a rigid schedule. It is always at the center of decision-making and can be very stressful. Diabetes can be even more difficult to manage when someone is also dealing with diabetes-related complications, other comorbidities and disabilities, or is a caregiver to others. Constant monitoring of blood sugar levels and frequent visits to health care providers were described as burdensome.

Respondents indicated that meal timing, intake, and food choices are restricted, which takes away from the pleasure of eating, and that it is demoralizing to always be receiving diet instructions from people (e.g., health care providers, family, strangers) about what they should be consuming and avoiding. Further, respondents said it is challenging to always be taking medication and to experience variability in blood sugar control. Several respondents spoke about the blame they inflict upon themselves for their disease, the shame and guilt they feel, and the stigma they experience. Some talked about how tough it is to interact with people who know very little about diabetes or who offer unsolicited advice about its management.

A majority of the respondents mentioned dealing with, and being apprehensive about, disease symptoms, medication side effects, and diabetes-related complications. Respondents described being chronically in pain and feeling tired a lot. They cited problems ranging from weight management issues, neuropathy and nephropathy, to amputations, changes to circulation and increased risk of heart attack, vision problems, and sexual changes. They reported living with depression and anxiety.

Respondents to the October 2016 survey indicated that they experienced the following symptoms and condition “sometimes” (“moderately”), “often” (“severely”) or “very often” (“very severely”) (n= 691):

- Hyperglycemia (75.1%)
- Hypoglycemia (38.1%)
- High blood pressure (51.1%)
- High cholesterol (48.2%)
- Heart problems (17.7%)
- Mental health problems (30.1%)
- Kidney symptoms or disease (18.8%)
- Foot problems (44.9%)
- Eye problems (41.5%)
- Nerve damage (37.4%)
- Damage to blood vessels, heart or brain (10.1%)
- Liver disease (9.4%)

People shared that diabetes has negatively affected their relationship and lifestyle. It has made it hard for them to work, travel, be flexible, and drive a vehicle – one respondent mentioned experiencing challenges with a driver’s license renewal because of diabetes. Diabetes decreases independence. People are fearful of complications and concerned about the long-term effects of the disease on their health, which can be emotionally taxing. They also mentioned the significant and overwhelming financial burden diabetes poses on themselves and their families.

Below are some quotes from survey respondents that further illustrate the degree and extent to which diabetes affects daily living and quality of life:

> *"Diabetes requires me to maintain a rigid schedule to ensure that my blood glucose levels are within a safe range. While at work, planning meetings and travel is harder as I have to have meals at regular times to ensure that my blood glucose levels don't go to low."*

> *"Takes lots of work to figure out when and what to eat. It is quite expensive for the medications I take and I am low income senior and I worry about that a lot."*

> *"These past couple of months I have very bad neuropathy[sic] pain in both feet...I do not have any med insurance so the costs of all of my drugs come out [of] our monthly income."*

> *"I've been a type 2 diabetic for almost 20 years now and I'm very frustrated with my health! I heal slowly, I get hungry quickly...I need more sleep, my skin is so dry no matter what I do...and I can't loose[sic] weight."*

> *"We liked to go to different restaurants and that is now limited as many do not have diabetic friendly[sic] food. Also there is a stigma associated with diabetes that others frown on things like taking your insulin in public…Never been able to see an educator for learning to use insulin, it has all been trial and lots of error, not much information available to starting on it."*

> *"DIabetes[sic] has resulted in the need for dietary changes for everyone in the house. I have neuropathic pain that sometimes makes it difficult to rest comfortably and to be as active as I normally would. I need to pay extra attention to my feet to make sure I don't have sores or infections, as they could take longer to heal than if I was not diabetic. I also have nephropathy, which I hope never progresses to chronic kidney disease."*

> *"I am a…mother…and hate the fact that I have developed diabetes and have to take medications for it. This disease gets in the way all the time (more trips to the doctor, more trips to the pharmacy, having to remember to take my medication and ensuring that I don't take too much medication so that I can drive my vehicle). My kids have to know what to do if I pass out, and that isn't the type of responsibility that young children should have."*

> *"I have neuropathy in my legs and hands. I have diabetic neuropathy in my eyes. I can't drive any more and have to rely on help from family and [an accessible transit service]. I was off for a year with Charcots[sic] foot. I walk with a cane now. Before this happened I was walking 5 kms[sic] a day. Im[sic] lucky if I get to the end of my driveway. Diabetes has taken away all my independence[sic]."*

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).

In the November 2019 survey, 11 respondents reported their experiences using anti-hyperglycemic agents. The medications being taken by respondents at the time the survey was completed included: GLP-1 receptor agonist (n=4), DPP-4 inhibitor (n=2), DPP-4 inhibitor combined with metformin (n=1), SGL2 inhibitor (n=5), sulfonylurea (n=1), metformin (n=6), and meglitinide (n=1). Further, seven respondents were taking insulin. A few respondents cited use of certain medications in the past. These included GLP-1 receptor agonist (n=4), DPP-4 inhibitor (n=4), DPP-4 inhibitor combined with metformin (n=1), sulfonylurea (n=5), metformin (n=3), and orlistat (n=1). Reasons for discontinued use of these medications were not provided.

There were ten respondents who provided input on how their current medications compare to their past medications. Of those respondents, at least 50.0% said they were “better” or “much better” able to meet target blood glucose levels during fasting period (n=9), upon waking (n=7),and after eating (n=8). Further, of the ten respondents, at least 50.0% said they were “better” or “much better” able to avoid hypoglycemia (n=5), meet target hemoglobin A1c (n=6), and maintain or lose weight (n=5). On current medications, the following were cited as “about the same as before” by at least 33.3% of respondents: the occurrence of bone fractures, urinary tract infections, lung or upper respiratory infections, thirst and/or dehydration, and maintaining or losing weight. Four of the respondents indicated that their ability to avoid hypoglycemia, gastrointestinal side effects, or occurrence of yeast infections was “worse” on their current medication compared to their previous medications.

There were 667 respondents who reported their experiences with antihyperglycemic agents in October 2016. The medications being taken at the time of survey completion included metformin (n=371), GLP-1 receptor agonists (n=312), SGLT2 inhibitors (n=165), combination of SGLT2 inhibitors and metformin (45), DPP-4 inhibitors (72), combination of DPP-4 inhibitors and metformin (147), sulfonylureas (n=140), TZDs (n=10), combination of TZDs and metformin (n=17), combination of TZDs and glimepiride (n=4), meglitinides (n=9), and acarbose (n=9). Many people reported taking insulin (n=309). A number of respondents indicated that they had experience with certain medications in the past as part of a clinical trial. Some reported stopping certain medications due to reasons other than the end of a clinical trial. The most commonly cited medications in this group were TZDs (n=97), sulfonylureas (n=94), GLP-1 receptor agonists (n=94), and DPP-4 inhibitors (n=92).

Over 60% of respondents to the October 2016 questionnaire noted improvements in meeting target blood glucose levels (fasting, post-prandial, upon waking) and hemoglobin A1c levels after initiation on their current medication regimen, compared to before (when they were not on treatment). Approximately 46% said they were “better” or “much better” able to avoid hypoglycemia, and 39% said their current regimen helped them maintain or lose weight more effectively than in the past. Gastrointestinal side effects were “neither better nor worse” than previously in 39 % of respondents. Close to two-thirds of participants indicated they were either “satisfied” or “very satisfied” with the medication or combination of medications they are currently taking for their diabetes management.

Below are direct quotes from respondents to the November 2019, Ocotober 2018, and October 2016 surveys that describe what they like and dislike about current therapy:

“Ease of administering them and their effectiveness.”

- 40-54 year old person with type 2 diabetes, diagnosed 1-2 years ago,

taking a GLP-1 receptor, SGLT inhibitor, and insulin.

“Its seeming to keep my blood sugar in a reasonable range most of the time”

- Person over 70 years old with type 2 diabetes, diagnosed 11-20 years ago, taking metformin and insulin.

“Nothing stands out though i[sic] would rather carry less meds in general if there were combined dosages.”

- Person with type 2 diabetes taking GLP-1 receptor agonist, SGLT2 inhibitor, metformin, and meglitinide.

“The insulin my husband takes helps control his blood sugar levels. He tests his blood sugar level 3 times a day and adjusts his food intake accordingly.”

- Caregiver to a person with type 2 diabetes taking metformin and insulin.

“Needles to administer insulin twice daily is[sic] painful but necessary. Current medications do not cause adverse side effects.”

- 55-69 year old person with type 2 diabetes, diagnosed 6-10 years ago, taking combination of SGLT2 inhibitor, and metformin, and insulin.

“[A GLP-1 receptor agonist] has so far been the best choice for me. The only dislike I have is that it causes the odd nausea and gut discomfort.”

- Person with type 2 diabetes taking a GLP-1 receptor agonist, metformin, and insulin.

“I have no [gastrointestinal] disturbance with my current melds[sic]. This is much better than when taking previous meds.”

- 55-69 year old person with type 2 diabetes, diagnosed more than 20 years ago, taking metformin and insulin.

“[A GLP-1 receptor agonist] has been excellent, has decreased very substantially my need for both basal and bolus insulin as well as other medications, reduced hypoglycemia and achieved weight loss.”

- Person over 70 years old with type 2 diabetes, diagnosed more than 20 years ago, taking a GLP-1 receptor agonist, SGLT2 inhibitor, metformin, and insulin.

“I have had poor control of my blood sugars over the years. I have tried products that either did nothing or caused more problems. [A GLP-1 receptor agonist] is assisting with better control. However, if my husband's health plan from work didn't cover it, I wouldn't be able to take it as the cost is about [a few hundred dollars] per. I take a lot of meds and wish I didn't have to.”

- 40-54 year old person with type 2 diabetes, diagnosed more than 20 years ago, taking a GLP-1 receptor agonist, metformin, and insulin.

“I feel like I take a huge amount of meds for diabetes and [a second health condition]. Its[sic] scary at times. As my benefits are capped, it is expensive - very. I'd like to say I feel great, but those days are rare.”

- Person diagnosed with type 2 diabetes taking an SGLT2 inhibitor, metformin, and insulin.

“There are so many of them [medications] and they cause a[sic] extreme dry mouth, nausea and diarrhea.”

- 40-54 year old person with type 2 diabetes, diagnosed 11-20 years ago, taking a GLP-1 receptor agonist, metformin, and insulin.

"I dislike the amount of injections that I have to take in order to maintain control over my sugar levels."

- 25-39 year old person with type 2 diabetes, diagnosed 6-10 years ago, taking a GLP-1 receptor agonist, metformin, and insulin.

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 asked about their expectations for new diabetes therapies, respondents to the November 2019, November 2018, and October 2016 surveys expressed a strong desire for medications that can normalize/stabilize blood glucose levels and improve hemoglobin A1c without causing weight gain or hypoglycemia. They wish for new treatments that have been proven to be safe, minimize side effects and damage to organs, and improve health outcomes. Patients want affordable drug options; ideally, they would like medications and diabetes devices to be covered by public and private plans. They want treatments that are easily administered, that cause the least amount of disruption to lifestyle, and allow for flexibility with food intake and choices. They also want medications that minimize the risk of diabetes-related complications and that avoid polypharmacy. Several respondents hope future treatments will reverse or cure diabetes.

Below is feedback from respondents indicating what they desire in new treatments, the improvements they would like to see made to therapies, and the impact these would have on daily life and overall quality of life:

"Allow for a better quality of life, while reducing side effects and damage to other organs and protecting/enhancing cardiovascular health."

"Able to assist in maintaining normal BG levels wile reducing the overall # of meds taken. Some point in the future to reverse the disease."

"Someday it would be lovely to just medicate once a month!"

"Hopefully easier attainment of targets, reduction of complication risks and less of a burden of disease."

"Improve diabetes control and health outcomes. I hope that these medications will be covered and available for all patients living with diabetes."

"I wish it was more affordable for the masses and covered by FNIHB [First Nations and Inuit Health Branch, Health Canada] for First Nation patients."

"Manage diabetes effectively without needing such a large variety of medications."

"Control glucose levels, cause little or no side effects, be reasonably priced."

"I hope that new drugs will eventually cure diabetes."

"I am hoping that the newer drugs are approved quicker by my insurance company."

"Expectations are that eventually there will be a medication that can be taken once a day that will help my pancreas produce the right amount of insulin to keep up with

me (or possibly even cure the disease). I would hope that medications are made available to anyone living with diabetes and covered under by our government benefits."

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.

Of those who participated in the November 2019 survey and responded to the questions specific to semaglutide (n=10), 30.0% reported taking semaglutide, 60.0% have never taken it, and 10.0% do not know whether they were on it. All three respondents who reported using semaglutide, indicated having switched to it from another medication and have their prescription covered through a private insurance plan. One respondent said semaglutide was better at helping them achieve their target hemoglobin A1c than previous therapies and one respondent said they did not know whether it was helping them achieve their target hemoglobin A1c. However, two respondents indicated that it was much better at helping them meet their target fasting blood glucose levels. One respondent reported semaglutide as "better" at helping them avoid low blood sugar and gastrointestinal side effects, while another responded indicated that it was "worse". Further, two respondents indicated that they were very satisfied with the use of semaglutide.

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.

TBC (semaglutide) does not have a companion diagnostic, therefore this question is not applicable to our submission.

8. Anything Else?

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

Diabetes is a disease that requires intensive self-management. Diabetes Canada's 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada highlight the importance of personalized care when it comes to the pharmacologic management of the condition. Specifically, after initiating healthy behaviour measures, the guidelines recommend selecting diabetes treatment modalities based on a patient's degree of glycemic control and various other considerations. To achieve optimal blood glucose levels, individualization of therapy is essential. This includes careful consideration of medication selection, route of administration (oral, injection, pen, or pump), frequency with which someone monitors blood glucose and adjusts dosage, benefits and risks that the patient experiences and/or tolerates, and lifestyle changes the patient is willing or able to make. Our survey responses reinforce the message that different people with diabetes require different medications/treatment modalities to help effectively manage their disease. Their unique clinical profile, preferences, and tolerance of therapy should direct physicians to the most appropriate choice and combination of treatments for their disease management.

Many people with diabetes hope for less dependence on medications. While current therapies have generally led to improvement for many people with diabetes in blood glucose and hemoglobin A1c control, respondents hope for even better, more affordable antihyperglycemic agents that they can access equitably, in a timely manner, and with good result to help them lead a normal life. Semaglutide may help people to achieve better glycemic control, which could potentially improve lives. For this reason, TBC (semaglutide) should be an option for people living with diabetes.

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.

   There was no assistance from outside Diabetes Canada to complete this submission.

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.

   There was no assistance from outside Diabetes Canada to collect or analyze data used in this submission.

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

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: Samantha Ghanem, MSc
Position: Manager, Health Research and Policy Analysis
Patient Group: Diabetes Canada
Date: December 11, 2019