B.C. PHARMACARE'S PUBLIC INPUT QUESTIONNAIRE
FOR DRUGS BEING REVIEWED UNDER THE B.C. DRUG REVIEW PROCESS

Drug Under Review: semaglutide (Ozempic)

Date Submitted: April 15, 2019 (deadline: May 1, 2019)

Confirmation of Eligibility

1. I am a representative of a patient group that represents patients in British Columbia who have the medical condition or disease which the drug under review would be used for AND the patient group which I represent has registered with PharmaCare to give input.
YES

Contact Information

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Conflict of Interest Declaration

6. Does your patient group have any Conflicts of Interest to declare?
YES

7. Describe any Conflicts of Interest below.
Diabetes Canada receives unrestricted educational grants from, among others, manufacturers/vendors of medications, supplies and devices for diabetes and its complications. These funds help the organization to support community programs and services for people with diabetes and contribute to research and advocacy efforts across Canada. No sponsor was involved in soliciting input for, or developing the content of, this submission.

Questions on the Drug Under Review

8. Have you read the PharmaCare information sheet for this drug?
YES, I have read the information sheet.

9. Describe how the medical condition or disease which the drug under review would be used for affects the day-to-day life of the patients in your group.

Diabetes is a chronic, progressive disease with no known cure. Type 1 diabetes occurs when the body produces either very little or no insulin. Type 2 diabetes occurs when the pancreas does not produce enough insulin and/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 each being potentially dangerous as an isolated event, 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.

This submission contains patient input from online surveys conducted in October 2016 and November/December 2018. Each survey was open for two weeks to people across Canada and consisted of a self-administered questionnaire. The surveys were directed at people living with type 2 diabetes and caregivers of people with type 2 diabetes and inquired about respondents' lived experience with diabetes and diabetes medications, and expectations for new drug therapies in Canada. The more recent of the two surveys posed a number of questions specifically about the drug under review, semaglutide (Ozempic). 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 e-mail subscribers through e-blasts

A total of 847 people participated in the October 2016 survey, with 86 reporting residence in British Columbia. Every respondent from British Columbia was over the age of 40, with the majority (67%, n=58) having lived with type 2 diabetes for over 10 years. Fewer people participated in the November/December 2018 survey (n=15) – there were 13 respondents who said they live with type 2 diabetes and 2 respondents who were caregivers to somebody with type 2 diabetes. A total of 6 people provided age and date of diagnosis data – 100% of respondents were over the age of 40 years, with 33% each in the 40-54, 55-69 and over 70 years age categories. The majority (n=4, 67%) reported having lived with diabetes for 6 years or more.

Two survey participants reported living in British Columbia, one person with type 2 diabetes and one caregiver.

In general, people surveyed talked about the negative impact diabetes has had on their lives. They reported constantly thinking about and planning around their disease, and talked about the stress this causes. They spoke about the ways that diabetes interferes with every aspect of life, from eating and exercising to working and socializing. People commented that diabetes makes it difficult to be flexible and spontaneous. Daily medication, constant monitoring of blood sugar levels and frequent visits to health care providers were described as burdensome. Respondents attested to the fact that diabetes is even more difficult to treat when someone is also dealing with comorbidity or disability.

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. People shared that diabetes has adversely affected relationships and decreased independence. They also mentioned the significant and overwhelming financial burden the disease inflicts on individuals and families.

Many people mentioned coping with, and being apprehensive about, disease symptoms, medication side effects and diabetes complications. Respondents described being chronically in pain and exhausted. They cited problems ranging from weight management issues, neuropathy and nephropathy, to amputations, changes to circulation, vision problems, and sexual difficulties, including erectile dysfunction. They also reported living with depression and anxiety.

Of the total responses from people living in British Columbia to questions about symptoms and disease complications in the October 2016 survey (n=86), the following were said to have been experienced “sometimes” (“moderately”), “often” (“severely”) or “very often” (“very severely”):

- hyperglycemia (74%)
- hypoglycemia (33%)
- high blood pressure (57%)
- high cholesterol (39%)
- heart problems (12%)
- mental health problems (22%)
- kidney symptoms or disease (13%)
- foot problems (54%)
- eye problems (41%)
- nerve damage (47%)
- damage to blood vessels, heart or brain (7%)
- liver disease (11%)

Of all those who responded to this question in the November/December 2018 survey (n=10), people experienced the following “sometimes” (“moderately”), “often” (“severely”) or “very often” (“very severely”):

- hyperglycemia (100%)
- hypoglycemia (50%)
- high blood pressure (70%)
- high cholesterol (60%)
- heart problems (20%)
- mental health problems (60%)

- kidney symptoms or disease (40%)
- foot problems (70%)
- eye problems (70%)
- nerve damage (70%)
- damage to blood vessels, heart or brain (40%)
- liver disease (10%)

Below are select quotes from British Columbians that demonstrate the challenges of living with diabetes:

"Life is very regimented…sometimes it can be frustrating to have no flexibility and always be on the same schedule, even on holidays."

"I am always having to keep track of my sugars and my food…I am concerned about my future and worry about complications."

"Taking medication is a part of my daily routine and if I for any reason miss taking it can suffer low blood sugars which is very unpleasant. Diabetes also has an impact on my vision, and…if my blood sugars are high or uncontrolled for any reason my vision is not clear and my eyes feel very tired."

"My mood is often flat or down, I am anxious about my health and taking medication while traveling is somewhat challenging."

"I am now experiencing problems due to long term diabetes such as heart issues and kidney problems."

"I can't eat whatever I want anymore. I have to remember to take medication. I have neuropathy in my feet."

"My fear is that I will not be able to afford [a particular antihyperglycemic agent] when I retire and no longer have medical coverage."

"I am concerned about further loss of health and possible complications in the future…I often get weary of the daily discipline required to manage diabetes daily in order to prevent or delay these possible future outcomes…I am concerned about possible financial hardships in the future. I currently have extended medical coverage for my medications but given how expensive some are…I may use up my lifetime maximum before I die and will have to cover much of the costs through my pension and savings."

"I have had type 2 diabetes for over 20 years. I think it has taken me that long to actually get it under control…I have found that family members try to understand but truly do not understand what a diabetic goes through everyday [sic]…The only one that truly understands is yourself."

"I'm very frustrated with my health!"

10. What drugs or other treatments have the patients in your group used, either now or in the past, to treat the medical condition or disease which the drug under review would be used for?

Past and present medication use

Many respondents reported antihyperglycemic agents being part of their past or present treatment history (or the history of the person for whom they provide care) in both surveys. A number of people mentioned having to take multiple medications as part of their prescribed regimen.

In the study conducted in October 2016, the following medications were reported as being currently in use by respondents from British Columbia: insulin, metformin, GLP-1 receptor agonists, SGLT2 inhibitors, a combination of SGLT2 inhibitors and metformin, DPP-4 inhibitors, a combination of DPP-4 inhibitors and metformin, sulfonylureas, acarbose, and meglitinides. Some respondents indicated that they had experience with certain medications in the past as part of a clinical trial (but are now no longer taking them). A small number reported stopping certain medications due to reasons other than the end of a clinical trial. The most commonly cited medications in this category were GLP-1 receptor agonists, TZDs, sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors and metformin.

In the more recent study conducted in November/December 2018, the following medications were reported as being currently in use by total respondents (n=6): metformin, GLP-1 receptor agonists, SGLT2 inhibitors, DPP-4 inhibitors, combination of DPP-4 inhibitors and metformin, and sulfonylureas. Insulin use was reported as follows: insulin glargine or insulin glargine biosimilar, insulin glargine U300 or other long-acting insulin, and intermediate-acting insulin. A few respondents mentioned use of certain medications in the past. These included DPP-4 inhibitors, combination of DPP-4 inhibitors and metformin, SGLT2 inhibitors, combination of TZDs and metformin, sulfonylureas, and metformin. Reasons for discontinued use of these medications were not provided.

Satisfaction with current therapy

Of those living in British Columbia who responded to this survey question in October 2016 (n=86), over 67% said they were “better” or “much better” able to meet their fasting blood glucose target, as well as their morning and post-prandial targets on their current antihyperglycemic therapy than before (without treatment). Close to 80% also stated that their current medication(s) helped them achieve hemoglobin A1c targets “better” or “much better” than previously. Between 13% and 27% of respondents reported the following as “somewhat worse” or “much worse” on their current regimen: gastrointestinal issues (nausea, vomiting, diarrhea, pain), ability to maintain or lose weight, thirst/dehydration and incidence of yeast infection/urinary tract infection.

When asked what factors were “quite important” or “very important” in choosing diabetes

medications, over 75% of respondents reported the following: keeping blood glucose at satisfactory levels during the day or after meals and upon waking or after fasting, avoiding low blood sugar during the day and overnight, avoiding weight gain/facilitating weight loss, reducing high blood pressure and risk of heart problems, and avoiding gastrointestinal issues (nausea, vomiting, diarrhea, pain), yeast infections, urinary tract infections, and fluid retention.

Of all those who responded to the question in the November/December 2018 survey (n=6), 50% said they were "better" or "much better" able to meet blood glucose targets upon waking and post-prandially on current antihyperglycemic therapy. On current medications, the following were cited as "about the same as before" by 50% or more respondents: meeting fasting blood glucose targets, maintaining or losing weight, gastrointestinal side effects, thirst and/or dehydration, yeast infection incidence and lung or upper respiratory infection incidence. A total of 33% of respondents said meeting target hemoglobin A1c level and post-prandial blood glucose targets and maintaining or losing weight was "worse" on their current medications than previously.

When asked what factors were "quite important" or "very important" in choosing diabetes medications, 83% of respondents said the following: keeping blood glucose at satisfactory levels during the day or after meals and upon waking or after fasting, avoiding low blood sugar during the day and overnight, avoiding weight gain/facilitating weight loss, reducing high blood pressure and risk of heart problems, and avoiding gastrointestinal issues (nausea, vomiting, diarrhea, pain), urinary tract and/or yeast infections, and fluid retention.

Below are some direct quotes from British Columbians who responded to the October 2016 and November/December 2018 surveys that describe what they like and dislike about their current therapy:

"Long acting [sic] meds are appreciated."
- 55 to 69 year old person with type 2 diabetes, diagnosed 11 to 20 years ago, taking metformin, a sulfonylurea, an SLGT2 inhibitor and insulin

"Better control of eating and blood glucose levels. Control of 'dawn effect'."
- 55 to 69 year old person with type 2 diabetes, diagnosed 6 to 10 years ago, taking metformin, a GLP-1 receptor agonist and insulin

"I strongly belief [sic] my quality of life has improved a lot."
- 55 to 69 year old person with type 2 diabetes, diagnosed 11 to 20 years ago, taking metformin, an SLGT2 inhibitor, a GLP-1 receptor agonist and insulin

"My current regime is working and isn't difficult."
- 40 to 54 year old person with type 2 diabetes, diagnosed 6 to 10 years ago, taking metformin, an SGLT2 inhibitor, a GLP-1 receptor agonist and insulin

"My day to day [sic] life has improved very much…I am no longer constantly thinking about food."

- 55 to 69 year old person with type 2 diabetes, diagnosed 11 to 20 years ago, taking an SGLT2 inhibitor, a GLP-1 receptor agonist and insulin

"[Medications] are very expensive."

- 55 to 69 year old person with type 2 diabetes, diagnosed more than 20 years ago, taking metformin, a sulfonylurea and a GLP-1 receptor agonist

"I don't like the injections."

- 40 to 54 year old person with type 2 diabetes, diagnosed 6 to 10 years ago, taking an SLGT2 inhibitor and a GLP-1 receptor agonist

"When I read about the side effects…I see that 'weight loss' is one…however, it's not happening in my case and I wish it would."

- 55 to 69 year old person with type 2 diabetes, diagnosed 11 to 20 years ago, taking metformin and a GLP-1 receptor agonist

"All meds so far have created more stomach upset than without."

- 40 to 54 year old person with type 2 diabetes, diagnosed 3 to 5 years ago, taking an SLGT2 inhibitor and a DPP-4 inhibitor

"I don't like that I have to take so many medications."

- 40 to 54 year old person with type 2 diabetes, diagnosed 6 to 10 years ago, taking metformin, a sulfonylurea and an SGLT2 inhibitor

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11. If the patients in your group have tried the drug under review, please tell us about the effects they experienced.

<u>Experience with semaglutide (Ozempic)</u>

Of those who participated in the November/December 2018 survey and answered the questions specific to semaglutide (Ozempic) (n=6), 50% reported taking semaglutide (Ozempic), 33% had no experience with it and 17% didn't know whether they were on it or ever had been. Two out of three people reported having switched to semaglutide (Ozempic) from another medication. One person was paying out-of-pocket for the medication, one had coverage through a private insurance plan and one received samples from his/her physician. Two people said semaglutide (Ozempic) was better at helping them achieve their target hemoglobin A1c than previous therapies, while one said it is worse. Two respondents reported semaglutide (Ozempic) as "better" or "much better" at helping them avoid low blood sugar, while one said it was the same as previous treatments. All three respondents said semaglutide (Ozempic) was the same or worse as previous treatments in terms of weight management properties and gastrointestinal side effects.

12. How do you think the patients in your group could benefit from using the drug under review? (For example: relief of existing symptoms; improvements in quality of life; or improvements to their condition and long-term health and well-being. Please provide details.)

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 medication 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 (Ozempic) may help people to achieve better glycemic control, which could potentially improve lives and save millions of dollars in direct health-care costs. For this reason, semaglutide (Ozempic) should be an option for people living with diabetes.

13. Are there any additional factors your organization would like PharmaCare to consider during its review of this drug? (For example: does the drug meet any special patient needs that have not been met by other drugs or treatments; is the drug easier to use than other drugs; does the drug reduce visits to the hospital; does the drug reduce days off work or school; or are the drug's side effects acceptable or intolerable?)

When asked about their expectations for new diabetes therapies, respondents to the October 2016 and November/December 2018 surveys expressed a strong desire for

medications that have been proven safe and can normalize/stabilize blood glucose levels and improve hemoglobin A1c without causing weight gain or hypoglycemia. They wish for new treatments to be affordable, enhance weight loss and improve health outcomes. Ideally, they'd like medications and diabetes devices to be covered in a timely manner by public and private plans. They want treatments that are easily administered, cause the least amount of disruption to lifestyle and allow for flexibility with food intake and choices. They also want medications that help them avoid polypharmacy and eliminate the need for injections while minimizing risk of any short-term medication-related side effects or long-term disease-related side effects. Several respondents hope future treatments will reverse or cure diabetes.

Below are quotes from British Columbian survey respondents who offered input on desired improvements to treatment and the impact these would have on their daily life and overall quality of life:

"I hope it will give people with type 2 diabetes a chance for better control towards normal."

"Help with neuropathic pain."

"Better overall blood sugar levels. More cost effective…fewer side effects."

"Lower blood sugar and weight loss."

"I hope that there will be a drug to help reduce weight without all the side effects of other weight loss drugs."

"Better control of problems. Fewer problems/reaction with meds. Cheaper. Work faster and better."

"Ultimately I would like to see a medication or therapy that would either eliminate type 2 diabetes or halt the damage that type 2 does to the bodily organs."

"Make it easier to keep glucose levels in the desired range. Have no or minimal side effects."

"Help cure people!"

"New and better understanding of the mechanisms of cause of type 2 diabetes will allow pharmaceutical companies to develop more efficient treatments that treat the cause of diabetes rather than just the symptoms. 'Boosting' the pancreas' ability to keep beta cell function and insulin production through better blood sugar control will allow healthier diabetics, with fewer costs to the healthcare system, and fewer complications overall."