

CADTH COMMON DRUG REVIEW

Patient Group Input Submissions

LIXISENATIDE (Adlyxine)

(Sanofi-aventis Canada Inc.)

Indication: As an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus in combination with:

- metformin
- a sulfonylurea (alone or with metformin)
- pioglitazone (alone or with metformin)
- a basal insulin (alone or with metformin)

when the therapy listed above does not provide adequate glycemic control.

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.

Diabetes Canada — permission granted to post.

CADTH received patient group input for this review on or before June 15, 2017

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.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Diabetes Canada

General Information

Name of the drug CADTH is reviewing and indication(s) of interest	lixisenatide (Adlyxine) Type 2 diabetes
Name of the patient group	Diabetes Canada
Name of the primary contact for this submission:	[REDACTED]
Position or title with patient group	[REDACTED]
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Website	www.diabetes.ca
Permission is granted to post this submission	Yes

Submitting Organization

Diabetes 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 organization 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, Diabetes Canada is delivering on its mission.

Conflict of Interest Declarations

Diabetes solicits and receives unrestricted grants from multiple manufacturers/vendors of pharmaceuticals, supplies and devices for diabetes and its complications. These funds help the organization to support community programs and services for people with diabetes, fund research and advocacy, across Canada. Sponsors were not involved in developing this submission. Diabetes Canada did not have any conflicts of interest in the preparation of this submission. The list of all sponsors is in the appendix.

Condition and Current Therapy Information

Information Gathering

Diabetes Canada solicited patient input through surveys distributed through social media and email blasts. Content of this submission is derived from surveys conducted in October 2016 and June 2017, which gathered information from Canadians with type 2 diabetes and their caregivers about the impacts of diabetes, experiences with current drug therapies and the drug under review. The first

survey was answered by 790 Canadians with type 2 diabetes and 57 caregivers who care for people with type 2 diabetes and the second survey was answered by 202 people living with type 2 diabetes and their caregivers.

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 prevent or delay complications.

The majority of respondents reported that diabetes had negatively impacted many aspects of their lives, having taken away flexibility, spontaneity and independence, particularly those who are suffering from diabetes-associated complications and those who experience difficulty controlling their diabetes. Many said diabetes has limited their ability to work and travel and social life. The burden was appropriately summed up by one respondent: "There is no "Day off", no holiday away from diabetes." Respondents also emphasized the psychological and emotional impact of diabetes as they experienced overwhelming stress and anxiety due to needed adjustments for diet and lifestyle, need for medications and associated side effects (i.e. weight gain), and daily burden of diabetes management. The cost of medications, supplies and healthy foods and a lack of understanding of diabetes in the society were cited as sources of stress as well.

When asked about comorbidities and symptoms, a majority of respondents said they had moderate or severe conditions below (in order of percentage):

- Hyperglycemia: 75%
- High blood pressure: 54%
- High cholesterol: 48%
- Hypoglycemia: 47%
- Eye problems: 43%
- Foot problems: 36%
- Nerve damage: 37%
- Mental health problems: 22%
- Kidney problems: 25%
- Heart problems: 17%
- Brain or blood vessels damage: 11%
- Liver disease: 9%

Patients' Experiences With Current Therapy

People with type 2 diabetes often cannot 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.

Canadians with type 2 diabetes and caregivers indicated broad experience with diabetes medications from Diabetes Canada's survey.

Medications being used

Given the small number of respondents who have taken each individual drug entity, the responses from patients who have used any type of GLP-1 receptor agonists, DPP-4 inhibitors and SGLT2 inhibitors have been combined to provide the most robust and comprehensive input.

The medications that respondents were taking at the time of survey include metformin (111), GLP-1 receptor agonists (11), insulin (160), SGLT2 inhibitors (31), sulfonylureas (29), DPP-4 inhibitors (30), TZDs (13), meglitinides (9), acarbose (9). Many people indicated having to take multiple medications as part of prescribed treatment.

Satisfaction with current therapy

As a result of diabetes medications, large percentages of respondents indicated they were better or much better at keeping blood glucose and A1C levels at target.

- 59% were better at meeting target fasting BG levels
- 51% were better at meeting target “upon waking” BG levels
- 44% were better at meeting postprandial BG targets
- 45% were better at avoiding hypoglycemia
- 56% were better at achieving target A1C levels

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.”

The vast majority 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
- blood sugars kept at satisfactory levels during the day/after meals
- avoiding low blood sugar during the day/overnight.

The following aspects are also considered important by the vast majority:

- avoiding weight gain,
- reducing heart problems
- avoiding GI effects,
- reducing high blood pressure.

Other aspects deemed important when choosing medications include “avoiding side effects”, “cost”, and “ease of administration” (injection versus oral). Some respondents simply wanted drugs “that are effective enough to allow for minimum, or no use, of other drugs” and provide a “life without concerns about complications because of diabetes.”

Information about the Drug Being Reviewed

Information Gathering

Diabetes Canada solicited patient input through surveys distributed through email blasts and social media. Conducted in both October 2016 and June 2017, these surveys provide information from Canadians with type 2 diabetes and their caregivers about their experience with GLP-1 agonists.

What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

Expectations of new medications

Among people with type 2 diabetes who answered our survey, almost all indicated it was important that the drug keep BG control, and most thought it was important to avoid hypoglycemia both during the day and overnight. Not gaining weight or losing weight, and reducing blood pressure and heart problems was a priority.

Many respondents spoke about the affordability of medications and management of diabetes. Some respondents preferred oral versus injected drugs: Injectables are “not as convenient as a tablet because it requires refrigeration and injection.” Many also would like new drugs to help “reduce the dependence on medications.” People also expect that new drugs will provide good mental health, more energy, no damage to organs, and “a feeling of overall wellbeing.”

Experience with GLP-1 receptor agonists

The majority of people who have experience with this class of drugs noted effectiveness in keeping blood sugar levels at target, achieving target hemoglobin A1C levels, and in some cases weight loss.

The majority of respondents indicated:

- their fasting BG levels were better
- their upon-waking BG levels were better
- their postprandial BG levels were better
- less hypoglycemia
- A1C improved
- better results in weight control

Of respondents with GLP-1 receptor agonist experience, many had switched from another medication, as a result of the need to gain better BG control. Most often this medication was added to current therapy to achieve better diabetes management outcomes.

Below are selected quotes on benefits experienced by people who have taken a GLP-1 receptor agonist.

“I have type 2 diabetes and also my husband and one of my sons. We were on secretalogues which would occasionally cause hypoglycaemia. We also had weight gain with these medications. Since we started [GLP-1 receptor agonist], we were able to come off the secretalogues, no more hypos and we have lost weight. We are controlling our diabetes much better, are much happier and satisfied with these results..”

“I was OK (well controlled) with glumetza (metformin) for about 10 years after my diagnosis, but my overnight, fasting figures were never great. Then my A1C figures started to rise and my doctor was worried so she added (sulfonylurea) and then (GLP-1 agonist) and now also (SGLT2 inhibitor). The combination has helped me to lose some weight and my A1C as well as my overnight fasting tests are better.”

While GLP-1 receptor agonists have been associated with many benefits and improved diabetes control, a significant percentage of respondents reported side effects such as extreme nausea and GI effects, some reported thirst or dehydration. Some respondents indicated they had to cut down the dosage of the drug to reduce side effects while keeping their A1C at range.

Summary

Diabetes is a disease 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 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, at affordable costs and hope for a healthy and longer life. Given the challenge that many people with type 2 diabetes have with weight loss and the enormous sense of failure associated with weight gain, diabetes medications that do not cause weight gain, and/or promote weight loss can be an important part of care.

The majority of people who have tried GLP-1 receptor agonists reported improved outcomes including BG and A1C control, weight loss, and decreased dependence on insulin and other medications. However, a significant number of people also reported side effects. The survey responses reinforce the understanding that different people with diabetes require different medications to help effectively

manage their disease. Their clinical profile, preference and tolerance of therapy can direct physicians to the most appropriate drug therapy. Based on reported benefits, lixisenatide (Adlexine) is an important option for some people with type 2 diabetes to achieve more effective management of diabetes and better health outcomes.