

CADTH REIMBURSEMENT REVIEW

Patient Input

HUMAN INSULIN (Entuzity KwikPen)

(Eli Lilly Canada Inc.)

Indication: Diabetes mellitus

CADTH received patient input from:

Diabetes Canada

February 22, 2021

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CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	Entuzity KwikPen (human insulin) Diabetes mellitus
Name of the Patient Group	Diabetes Canada
Author of the Submission	██████████
Name of the Primary Contact for This Submission	██████████
Email	████████████████████
Telephone Number	██████████

1. About Your Patient Group

Describe the purpose of your organization. Include a link to your website.

Diabetes Canada is a national health charity representing over 11 million Canadians living with diabetes or prediabetes. The priorities of our mission are diabetes prevention, care and cure. Our focus on research and policy initiatives helps us to deliver impact at a population level, and our partnerships broaden our reach in communities across the country. We drive excellence in disease management by putting practical, evidence-based tools into the hands of health-care providers. We advocate for environments that make the healthy choice the easy choice. We continue our search for a cure, as well as for better prevention and treatment strategies, by funding the work of innovative scientists. In 1921, Canada changed diabetes for the world with the discovery of insulin. In 2021, we will 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 an online survey conducted in January/February 2021. It was open for two weeks (January 29-February 12) to people across Canada of all ages with type 1 or type 2 diabetes and their caregivers. It consisted of a self-administered questionnaire of

closed- and open-ended questions about respondents' lived experience with diabetes and diabetes medications (with specific questions about the drug under review, Entuzity), and expectations for new drug therapies in this country. It was advertised through Diabetes Canada's social media channels (Facebook, Twitter, Instagram and LinkedIn), by e-mail through a monthly newsletter to members of the Diabetes Canada Professional Section and through a post on the health-care professional discussion platform TimedRight.

A total of 48 people participated in the survey – 26 identified as living with type 1 diabetes and 19 with type 2 diabetes, while 3 said they were caregivers (1 to somebody with type 1 diabetes and 2 to somebody with type 2 diabetes). Respondents resided in Newfoundland, Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta and British Columbia, with the most representation from Ontario (n=21) and British Columbia (n=12). Respondents' ages ranged from under 18 (n=2) to 75 years and over (n=3), with 79% of people reporting being at least 35 years old and the biggest concentration of respondents (n=14) falling in the 35-44 year grouping. About 27% (n=13) reported living with diabetes for 10 years or less (with 5 having had it for less than 1 year). There were 15 respondents who have been living with diabetes for 11-20 years and the largest proportion (42%, n=20) having had diabetes for more than 20 years.

Of those who responded to the question, 10 people (21%) reported having experience with the drug under review, Entuzity. In total, 7 people said they currently take Entuzity along with other diabetes medications (1 person with type 1 diabetes, 6 people with type 2, all over the age of 35 years and all with diabetes for at least 11 years), while 3 said they only take Entuzity for their diabetes management (1 person with type 1 diabetes, 2 people with type 2, all over the age of 45 years and all with diabetes for more than 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 of different types, but none with any known cure. Common symptoms of diabetes include extreme fatigue, unusual thirst, frequent urination and weight change (gain or loss). Approximately 5-10% of people with diabetes live with type 1. Type 1 diabetes occurs when the pancreas does not produce its own insulin; to survive, daily exogenous insulin by injection or infusion is required. About 90% of those diagnosed with diabetes live with type 2. Type 2 diabetes occurs when the pancreas does not produce enough insulin or the body does not effectively use the insulin that is produced. Treatment may include insulin, in addition to other therapies. Typically type 1 diabetes presents in children and adolescents, while type 2 develops in adulthood, though either type of diabetes can be diagnosed at any age. The drug under review, Entuzity, is indicated for adults and children living with type 1 or type 2 diabetes.

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. Suboptimal glucose control can be quite serious and problematic to health. Low blood glucose can precipitate an acute crisis, such as confusion, coma, and/or seizure that, in addition to being dangerous, 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. One important goal of diabetes

management is to keep glucose levels within a target range to minimize symptoms and prevent or delay complications.

When asked about the effect of diabetes on day-to-day activities and overall quality of life, a few respondents expressed that it doesn't impact them much. One person stated "generally controlled diabetes can relatively leave you with a normal life". But the vast majority talked about how challenging, preoccupying, time-consuming and worrisome it is to live with diabetes. Respondents characterize diabetes as a burden, saying things like "I struggle" and "I suffer" to describe their experience. One person said "it affects every single thing every day". Another said it "governs everything I do". A third said "every decision made is impacted by the disease".

Several described diabetes as a condition that must be dealt with 24 hours a day/7 days a week/365 days a year with no breaks and no holidays or time off. It is physically and mentally exhausting. Respondents mentioned that testing, medication adjustment and equipment set up and use all take lots of time. Planning eating occasions, making food choices and counting carbohydrates can be difficult. While exercise can assist with management, it also must be managed. Respondents talked about how expensive diabetes is to live with. People feel unwell a lot, particularly when blood sugars are variable. Some reported living with complications that are painful, upsetting and bothersome. Others mentioned the toll diabetes takes on mental health. They shared accounts of feeling anxious, concerned about the future, stigmatized, shamed and blamed. One person said "I always worry about my health".

When asked specific questions about comorbidities and health issues, respondents cited having the following:

- weigh management concerns (67%)
- high blood pressure (54%)
- mental health concerns (31%)
- abnormal cholesterol levels (31%)
- eye problems (31%)
- foot problems (29%)
- kidney issues/kidney disease (21%)
- heart condition/heart disease (19%)

Other symptoms, issues and conditions were reported by 21% of respondents, including arthritis, fatty liver, digestive problems, fibromyalgia, chronic fatigue, headaches, nausea, diarrhea and epilepsy.

Below are some quotes that further illustrate respondents' lived experience with diabetes and its effect on daily life and quality of life:

"It impacts every decision I make. It impacts what I eat, how much I eat, whether or not I have enough insulin to eat my whole meal. It impacts how I sleep, how tired I am, how much I can exercise."

"My...daughter was diagnosed in...2020, it's affected our daily life...It [sic] a very scary thing to think your child could die if your [sic] not doing your job as a parent. It has effected [sic] us financially as well and we don't have any of the fancy devises [sic] because our insurance won't cover them."

"Constant testing, setting up insulin pump, counting carbs and adjusting insulin needs based on illness, menstruation, comorbidities. Mental health struggles as well with acceptance, self care burden, and the impact of blood sugars on mood, anxiety about future ability to care for self, and increase of comorbidities and complications. Decreases overall money through inadequate coverage of diabetes technology and supplies, and the burden of meeting Pharmacare deductibles. Stigmatization and disrespect from others based on T1D diagnosis and daily care needs."

“I suffer from bouts of depression and burnout.”

“Lots of Numbness [sic], Tiredness [sic].”

“As a family member, I’m always worried about related complications that might take place when glucose levels are high.”

“Often interferes with my work...hard to plan diet around a dynamic job, constant stress due to diabetes concerns, frequent depression, sick days interfere with work and life, cannot get insurance.”

“Diabetes is tiring. Constant carb counting. Constant vigilance for glucose. High sugars. Low sugars. Disapproval from outsiders re what I eat and how I should live my life.”

“I am not that old person, but due to diabetes, I feel older than ever before and it’s pretty hard to balance it.”

“I have a young family, I work [a job] which commands a ton of my time and attention. I have little to no time to allocate to myself, yet, Diabetes [sic] is a full time job.... It can be crippling at times.”

“It revolves around everything I do, when I wake up, what I eat, how I eat, when I eat. If I want to exercise or lose weight I have to factor these things in or else I get a sugar low and again have to eat something which makes you feel defeated. Always prepping for where you will be, for how long, do I need to bring a snack, my insulin? Can I take my shot or check my sugar without other people looking?”

“I use a sensor because I cannot feel my low blood sugars anymore. I have to calibrate it by checking my blood sugar 3 times a day minimum and pay a lot of money for sensors, which I have to change every 6 days or less. It is a constant struggle to keep blood sugars in range, otherwise I may feel horrible for seemingly no reason. It affects everything I eat, because I have to account for it using insulin to balance things off, but it can be a bit of a guesstimation game when it comes to calculating carbs. Overall I never forget that my diabetes is there, affecting everything I do and feel.”

“Exercise, food, stress, and other illnesses all make it difficult to manage blood sugars. And with unmanaged [blood sugars] you just feel worse. It’s a balancing act and very difficult and unpredictable.”

“I have a very limited diet and that causes frustration. If my blood numbers get high for no apparent reason it cusses [sic] a lot of stress. I worry about long term effects of the disease.”

“It makes life much more difficult, I don’t feel well most of the time, weight gain is a big problem, my feet are causing walking to be very difficult. Cost is a factor. Its [sic] very inconvenient having to give myself injections 3 [times] a day. Some of the tools offered for checking blood without using the test strips are too expensive for me. In my opinion it would be nice if the Government [sic] was more helpful with the costs of diabetes.”

“Anxiety, having to take needles and careful watch of sugar levels, insulin to administer can be tiring and stressful. Kids are sometimes afraid if I have a low. That is worrying. My husband’s constants [sic] concern with what I am eating, did I take my insulin, etc.”

“Painful injections of insulin 4 times every day. Costs of supplies are very expensive, comes out of my limited budget. Concerns about dying prematurely.”

“I’m struggling to manage effects and big changes with diet.”

“Not able to eat what you want when you want. Unable to walk or hike far due to blood sugars and diabetic ulcer. Mood swings when blood sugars are too low and unable to just relax and enjoy life.”

“It is frustrating that there is no cure for type 1 yet. It is very difficult to constantly try to control your blood sugar.”

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).

There were 45 respondents who reported experience with antihyperglycemic agents to manage their diabetes. The oral and injectable medications being taken at the time of survey completion included:

- GLP-1 receptor agonists
- DPP-4 inhibitors and metformin
- SGLT2 inhibitors
- sulfonylureas
- metformin
- insulin

Respondents had experience with the following types of insulin:

- glargine or glargine biosimilar
- glargine U300/other long-acting
- intermediate-acting
- short-acting
- rapid-acting

Of the 45 respondents who answered this question, 29% reported being “very satisfied” with the medication they are currently taking for their diabetes management and 47% reported being “somewhat satisfied”. Another 13% said they were “neither satisfied nor dissatisfied” with their medication, while 11% said they were “somewhat dissatisfied” or “very dissatisfied”. When asked what they like about their medications, respondents cited the following:

- effectiveness/ reasonable control of blood sugar
- efficiency/speed with which it works
- freedom to carry and use medication anywhere
- works with a pump
- facilitates weight loss
- improvements to blood sugar and hemoglobin A1c
- improvements to liver and kidney function

A few people said that their diabetes medications keep them alive, and that this is less of a ‘feature’ of the medication that they like, but more a necessity for survival.

Respondents said they dislike the following about their medications:

- having to inject
- having to take big doses
- the length of time it takes the medications to work
- the fatigue they cause
- multiple daily injections
- having to take them daily
- the size of tablets

- the high cost
- the frequency of monitoring that accompanies medication use
- side effects

Respondents commented on several side effects experienced on their medications, including, but not limited to, yeast infections, urinary tract infections, weight gain, fatigue, hypoglycemia, arrhythmias, gastrointestinal issues (stomach upset, diarrhea), loss of appetite, bruising around injection site, thirst, lightheadedness, depression and “brain fog”.

Many felt their current medication regimen is helping them better meet fasting blood sugar target levels and those measured upon waking and after meals, as well as their target hemoglobin A1c. Many felt the medications they are taking now were neither better nor worse than ones previously taken with respect to weight maintenance or loss and problems like gastrointestinal issues, thirst/dehydration and infections (yeast, urinary tract). Most respondents said they don’t have any issues obtaining their medications, though some pointed out that they are costly or not covered by their insurance, which are significant barriers. One person said “medication is so expensive so sometimes I have to conserve insulin use”. Another said “each time it takes me 1.5 hours for return driving” to obtain a prescription refill.

Respondents who answered this question (n=12) reported the following considerations as “very important” when choosing pharmacotherapy for diabetes management:

- keeping blood glucose at satisfactory level during the day or after meals: 91%
- keeping blood glucose at satisfactory level upon waking or after fasting: 91%
- avoiding low blood sugar during the day: 75%
- avoiding low blood sugar overnight: 79%
- avoiding weight gain/reducing weight: 63%
- reducing high blood pressure: 61%
- reducing risk of heart problems: 63%
- avoiding gastrointestinal side effects (nausea, vomiting, diarrhea, abdominal pain): 56%
- avoiding urinary tract and/or yeast infections: 56%
- avoiding fluid retention: 61%

Below are some direct quotes from respondents that describe the things that are important to them when choosing a diabetes medication:

“The ability to be used with an insulin pump.”

“The simpler the better.”

“Convenient [sic] and effective.”

“No weight gain, minimum number of pills.”

“Long term affordability for people without insurance.”

“Ease of use.”

“Trusted by medical team.”

“The ability to manage and change my dosages as needed.”

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?

Respondents would like to see the following in diabetes treatments:

“All devices that help track and inject insulin...should be covered for all children [sic].”

“Faster working insulin’s [sic].”

“Not having to take needles would be nice, fewer side effects of meds.”

“Get something to deliver insulin easier.”

“More information about new happenings with diabetes treatments.”

“Reduce amount of potential side effects.”

“Better pump technology.”

“Less injections per day.”

“To not need medication. Advance medical care.”

“A cure, plain and simple.”

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.

There were 10 respondents who reported experience with the Entuzity KwikPen. A total of 5 respondents said the medication was covered in full or part by private insurance, while others said they had to pay the full cost of out pocket (n=1), were able to get the medication through a clinical trial (n=1), obtained manufacturer’s samples (n=1) and accessed it other ways (n=2).

People shared the following comments about what they like about Entuzity:

“Ease of use.”

“I love how it controls my glucose levels without the need to increase volume. Checking my blood sugar levels several times a day. You notice the medication working. Less spikes.”

“It’s quick and easy.”

“Helps me control my blood sugar levels to the point of being almost normal.”

“Concentration allows 1 pen to last about a week when u100 or u200 would only last 2-3 days max.”

“Highly recommended.”

“No need to measure.”

Respondents cited disliking the fact that they require multiple daily injections and that the cost is high. Otherwise, people said they are “100% satisfied”, “like the pen” and “u500 [sic] has been a real game changer”.

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.

Entuzity does not have a companion diagnostic.

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 treatments 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, infusion), 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 prescribers to the most appropriate choice and combination of treatments for disease management. Health-care providers must be supported in prescribing evidence-based therapies and, through public and private drug plans, patients should have access to a range of treatments that will allow them to optimize their health outcomes. For those paying out-of-pocket, costs should not be so high as to prohibit medication procurement.

While current therapies have generally led to improvement for many people with diabetes in blood glucose and hemoglobin A1c control, respondents hope for additional affordable agents that they can access equitably, in a timely manner, and with good result to help them lead a normal life. Entuzity may help people to achieve better glycemic control, which could potentially improve lives and save millions in direct health-care costs. For this reason, Entuzity 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 reimbursement review process, 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.

Diabetes Canada had no outside assistance 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.

Diabetes Canada had no outside assistance 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

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 support community programs and services for people living 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.

Please see the attached list of Diabetes Canada's financial contributors.

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: Ann Besner, MScA, RD
 Position: Manager, Research and Public Policy
 Patient Group: Diabetes Canada
 Date: February 22, 2021

Diabetes Canada Financial Contributors

Last updated: February 2021

\$400,000+



\$150,000 - \$399,999



\$50,000 - \$149,999



\$20,000 - \$49,999

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