



Common Drug Review *Patient Group Input Submissions*

Alogliptin Plus Metformin (Kazano) for Diabetes Mellitus (Type 2)

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

Canadian Diabetes Association — permission granted to post.

CADTH received patient group input for this review on or before August 28, 2014

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. This includes patient input received from individual patients and caregivers as part of that pilot project.

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.

Canadian Diabetes Association

Section 1 – General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Alogliptin plus metformin (Kazano) for Diabetes mellitus (Type 2)
Name of patient group	Canadian Diabetes Association
Name of primary contact for this submission:	[REDACTED]
Position or title with patient group	[REDACTED]
Email	[REDACTED]
Telephone number(s)	[REDACTED]
Name of author (if different)	
Patient group's contact information:	Canadian Diabetes Association
Email	advocacy@diabetes.ca
Telephone	613-688-5938
Address	45 Montreal Road Ottawa, ON, K1L 6E8
Website	www.diabetes.ca
Permission is granted to post this submission	Yes

1.1 Submitting Organization

The Canadian Diabetes Association (the Association) leads the fight against diabetes by helping people with diabetes live healthy lives while we work to find a cure. It has a heritage of excellence and leadership, and its co-founder, Dr. Charles Best, along with Dr. Frederick Banting, is credited with the co-discovery of insulin. The Association is supported in its efforts by a community-based network of volunteers, employees, health care professionals, researchers, and partners. By providing education and services, advocating on behalf of people with diabetes, supporting research, and translating research into practical applications, the Association is delivering on its mission.

1.2 Conflict of Interest Declarations

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

Section 2 – Condition and Current Therapy Information

2.1 Information Gathering

The Canadian Diabetes Association (the Association) solicited patient input through a survey distributed through social media and email blasts. The survey was open for approximately 2 weeks and included questions on how diabetes impacts the lives of patients, current drug therapy, previous experience with drug therapy and experience with Nesina (alogliptin) and Kazano (alogliptin and metformin). Among the 388 individuals who responded, 92.8% identified themselves as patients living with type 2 diabetes, 4.1% as caregivers for someone with type 2 diabetes, 0.5% as having type 1 diabetes, and 2.6% as other. The survey data reported in this submission are from those people living with diabetes or caring for someone with type 2 diabetes (n=376). Of those 376 responding 93% are taking (or had taken) diabetes medication. Approximately 27% had taken DPP-4 inhibitors (including alogliptin (Nesina)), and 8.5% (n=14) have taken combination alogliptin and metformin (Kazano). Approximately 30% stated having direct experience with DPP-4 inhibitors. A total of 250 respondents completed the full questionnaire with a range from 388 to 250 respondents for individual questions.

The call for patient input for Nesina (alogliptin) and Kazano (combination of alogliptin and metformin) were made at the same time. Given the patient experience for these drugs will be similar, this submission should be considered for both review processes.

Current clinical data suggests the similarity of the DPP-4 inhibitor drugs. Given the small number of respondents who have taken each individual drug entity, the responses from patients who have used any type of DPP-4 inhibitors have been combined to provide the most robust and comprehensive input.

2.2 Impact of Condition on Patients

Type 2 diabetes is a chronic (progressive) condition that occurs when the pancreas does not produce enough insulin or when the body does not effectively use the insulin that is produced. Insulin is a hormone that controls the amount of glucose in the blood. Common symptoms of diabetes include fatigue, thirst and weight change. High blood glucose levels can cause long-term complications such as blindness, heart disease, kidney problems, nerve damage and erectile dysfunction. The goal of diabetes management is to keep glucose levels within the target range to minimize symptoms and avoid or delay the complications.

Diabetes requires considerable self-management, including healthy eating, regular physical activity, healthy body weight, taking diabetes medications (oral and/or injection) as prescribed, monitoring blood glucose and stress management. Poor glucose control can result in serious long-term complications.

Patients in the survey were asked which aspects of diabetes were the most important. The majority of patients indicated that daily fluctuations in blood sugar were the most important aspect of diabetes to control during the day and overnight. The fluctuations impact the ability to work, interactions with friends and family, causes stress and worry as well as ability to participate in normal activities of daily living. Uncontrolled diabetes and the stigma associated with the disease can result in reduced quality of life. Maintaining control of diabetes has potential to reduce anxiety and avoid or delay complications as well as improve overall quality of life.

There was a frequent emphasis on the psychological and emotional impact of diabetes on the lives of respondents (effect on stress, anxiety, adjusting to changes in diet and lifestyle, medication and treatment management as well as relationships with family). Respondents also described fatigue, and lack of energy.

“Having diabetes makes me useless. I have no energy or strength to enjoy life anymore. I can’t do partial jobs around house. I can’t enjoy sports anymore. Diabetes has instill (sic) a fear in me.”

Management of diabetes includes lifestyle changes (diet, exercise and stress management). Inevitably, most patients are prescribed one or more medications to achieve glucose control. This usually starts with metformin (oral agent) and, if target glucose levels are not met, other medications are added. Over time most patients will be treated with multiple diabetes medications in order to achieve glycemic control. Many patients with diabetes do not take oral glucose-lowering therapy as prescribed. Almost 30% of respondents found it somewhat difficult, difficult, or very difficult to take multiple medications through the day to manage diabetes. This finding is validated by the medical literature. Poor adherence has been associated with loss of glycemic control, increased risk of complications and costs in patients with type 2 diabetes.

2.2.1 Selected quotes from respondents when asked about challenges related to diabetes

“It is a life altering disease that impacts every aspect of life. There is constant blood monitoring, diet, level of activity, cost of expensive supplies and medication.”

“I’m always afraid my husband’s sugar will fall too fast.”

“having to take multiple medications, constantly aware of what foods you eat, insomnia, insulin injections, and blood testing.”

“I have to watch my diet somewhat. My biggest concern is the number of medications I take as a result of being diabetic.”

“Basically it’s an awful experience, experience highs and lows. Exercising can make my sugars low so I have to always have a snack with me. Eating anywhere besides home is a challenge as you don’t know how things are made. I’m constantly checking my blood and I take 13 pills a day.”

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

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

2.3 Patients’ Experiences With Current Therapy

A large proportion of people with type 2 diabetes fail to achieve optimal glycemic control, which places patients at risk for both acute and chronic diabetes complications. Initial therapy is most often with metformin, but over time, most patients will require the addition of a second or third agent to reach glycemic targets. Many of the currently available second-line therapies cause significant weight gain while their ability to achieve optimal glycemic control may be limited by hypoglycemia.

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

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

Respondents were asked to provide, in their own words, the benefits and side effects of their drug therapy, and the responses were examined separately for those with DPP-4 inhibitor experience and those without experience. All responses were categorized by theme and then grouped by sub-themes. The majority of those with DPP-4 inhibitor experience reported they were mostly satisfied with drug therapy (similar to overall response) and with the fact that their blood sugar levels were kept at target. Many patients indicated frustration with having to take multiple medications, including drugs to maintain blood sugar, hypertension, cholesterol lowering agents and others. Several respondents identified previous prescribed drugs as having intolerable side effects – mostly hypoglycemia, morning hyperglycemia and gastrointestinal effects. There were no specific side effects experienced with DPP-4 inhibitors and respondents qualitatively indicated satisfaction with control and but some indicated frustration with lack of control. Most of the concerns raised from respondents were related to the need for multiple medications, cost of treatment, and lack of insurance coverage.

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

Section 3 – Information About the Drug Being Reviewed

The availability of alogliptin offers patients an alternative treatment option for stabilizing blood glucose. Kazano further offers a fixed dose combination of metformin with alogliptin for patients stabilized on previous therapy of metformin, alogliptin (with a SU or insulin) and would serve additional benefit of effective therapy while reducing pill burden and promoting adherence. This would translate into a significant advantage for doctors and patients working together to achieve optimal treatment with the lowest effective dose.

Respondents were asked to rate their level of knowledge of the Nesina (alogliptin)and Kazano (alogliptin plus metformin), regardless if they have taken the drug using a four-point scale from “have not heard about” to “know a lot about”. Respondents had very little knowledge of Nesina 95% having little or no knowledge; 86% of respondents had little or no knowledge of Kazano. Most with no exposure to the DPP-4 inhibitors had little or no expectations for these drugs. Among those with experience, the most frequent expectation was to have better blood glucose control, including fewer instances of hyperglycemia and hypoglycemia. While most indicated the expectation of fewer side effects (including hypoglycemia and weight gain), others indicated they worry about side effects of medications.

Survey respondents were asked how important is it to have a drug (Nesina or Kazano) available for treatment of diabetes?

Patients responded overwhelmingly with approximately 75% stating that availability is important. Qualitative responses were also provided, for example

“To give patients the best options for managing their health”

“We need to be able to make an informed decision and have the power to make our own choices! It’s about our mental health and wellness to!!”

With respect to the benefits of a combined therapy with Kazano, respondents were asked to what degree is it difficult to take multiple drugs?

Approximately 30% indicated that they found it difficult to take multiple medications. This is significant considering that these patients are also experiencing high rates of co-morbid conditions such as hypertension, heart failure, depression, renal disease, and others. Simplifying the drug regimen is a serious and important issue for this patient population.

In summary, diabetes is a very common chronic progressive condition that requires intensive self-management. To achieve optimal blood glucose levels, individualization of therapy is essential, including selecting the drug or combination of drugs, route of administration (oral, injection, pen or pump), how frequently the patient monitors blood glucose and adjusts dosage, the benefits and risks that the patient experiences and/or tolerates, and the lifestyle changes the patient is willing or able to make.

There are clear expectations among respondents that drugs should offer better blood glucose control. Patients with DPP-4 experience collectively stated good results from DPP-4 use. Patients expressed frustration with the weight gain associated with metformin use. A substantial proportion of patients identified taking several medications as a concern, and when asked if a pill that combined two medicines should be made available, respondents were very supportive. Responses to this survey reinforce the understanding that most patients are required to make several changes in their lifestyle and drug regimen over the course of their disease. Their preference and tolerance of therapy is influenced by many individual factors. The availability of the DPP-4 inhibitors provides an important option for patients, especially when metformin alone is no longer effective. It may promote adherence to treatment by reducing pill burden and can offer some patients a good alternative for effective treatment of diabetes.

Section 4 – Appendix

Organizations and foundations that made donations to the Canadian Diabetes Association between September 2012 and August 2013.

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