CADTH

CADTH COMMON DRUG REVIEW

CADTH Canadian Drug Expert Committee Recommendation

(Final)

Lixisenatide (Adlyxine — Sanofi-aventis Canada Inc.)
Indication: Diabetes mellitus, type 2

Recommendation:
The CADTH Canadian Drug Expert Committee (CDEC) recommends that lixisenatide be reimbursed for use as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus if the following criterion and condition are met:

Criterion:
- Lixisenatide should be used only in combination with a basal insulin (with or without metformin).

Condition:
- Drug plan costs for lixisenatide should not exceed the drug plan costs of the least costly pharmacotherapy reimbursed for the treatment of type 2 diabetes mellitus in combination with a basal insulin (with or without metformin).

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Redactions: Confidential information in this document has been redacted at the request of the manufacturer in accordance with the *CADTH Common Drug Review Confidentiality Guidelines.*

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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- Lixisenatide should be used only in combination with a basal insulin (with or without metformin).

Condition:

- Drug plan costs for lixisenatide should not exceed the drug plan costs of the least costly pharmacotherapy reimbursed for the treatment of type 2 diabetes mellitus in combination with a basal insulin (with or without metformin).

Reason for the Recommendation:

1. In four double-blind, placebo-controlled phase III randomized controlled trials (RCTs), lixisenatide in combination with basal insulin (alone or with metformin) was superior to placebo in decreasing glycated hemoglobin (A1C) levels over 24 weeks in adult patients with type 2 diabetes mellitus. In one open-label, active-controlled RCT, lixisenatide in combination with basal insulin (with or without metformin) was noninferior to insulin glulisine once daily and insulin glulisine three times a day in decreasing A1C over 26 weeks.

Of Note:

- CDEC noted that there is a high degree of uncertainty associated with the cost-effectiveness results of lixisenatide based on the limitations identified in the economic analysis, particularly regarding the dose and price of prandial insulin, as well as utility decrements for hypoglycemic events. There is also substantial uncertainty in the actual dose of prandial insulin over time and with extrapolating the short-term effects prandial insulin and lixisenatide observed in clinical trials to a lifetime time horizon.

Discussion Points:

- CDEC noted that the ELIXA study demonstrated noninferiority — but not superiority — of 20 mcg lixisenatide compared with placebo on the composite outcome of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalization for unstable angina in patients with type 2 diabetes mellitus who recently experienced a spontaneous acute coronary syndrome event. Use of basal insulin was not an inclusion criterion for the ELIXA study. In light of emerging evidence regarding the efficacy of some hypoglycemic agents in reducing major adverse cardiac events, the lack of superiority for lixisenatide may indicate that it has a limited role in this population.
- CDEC noted that both the clinical and pharmacoeconomic evidence were based primarily on A1C effects and extrapolation (in the pharmacoeconomic model) of those effects to clinical outcomes. While this is consistent with previous assessments of agents for the treatment of diabetes mellitus, this extrapolation is being reconsidered given the emerging cardiovascular outcomes studies.
- CDEC noted that there was no evidence to suggest that lixisenatide meets a need that is not currently met by existing treatment options. The committee considers lixisenatide to be another option for patients who are not adequately controlled on existing therapies.
- CDEC noted that lixisenatide was shown to have more frequent adverse events compared with the placebo group in all placebo-controlled trials. The most commonly reported adverse events that occurred more frequently in the lixisenatide treatment groups compared with the placebo groups were consistent, and common to, the gastrointestinal risk profile of glucagon-like peptide-1 receptor agonists.

Background:

Lixisenatide is a glucagon-like peptide-1 receptor agonist and has a Health Canada–approved indication as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus in combination with the following therapies when they do not provide adequate glycemic control:

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

The recommended starting dose of lixisenatide is 10 mcg once daily for 14 days, administered subcutaneously (in the thigh, abdomen, or upper-arm) within the hour prior to any meal. Lixisenatide should be administered before the same meal every day. The dose should be increased and maintained at 20 mcg once daily on day 15 and thereafter for additional glycemic control. The maximum recommended dose is 20 mcg once daily. Lixisenatide is available as a pre-filled pen in strengths of 0.05 mg/mL, and 0.1 mg/mL to deliver 14 doses of 10 mcg per dose or 20 mcg per dose, respectively.

Summary of CDEC Considerations:

CDEC considered the following information prepared by the CADTH Common Drug Review (CDR): a systematic review of RCTs of lixisenatide, a critique of the manufacturer's pharmacoeconomic evaluation and patient group-submitted information about outcomes and issues important to patients with type 2 diabetes mellitus.

Patient Input Information:

One patient group, Diabetes Canada, responded to the CDR call for patient input. Information for the patient input submission was obtained from online surveys. The following is a summary of information provided by the patient group:

- Patients require considerable self-management, including diet, physical activity, body weight, blood glucose, and stress in addition to diabetic medications.
- Inadequate control of blood glucose can lead to a range of serious comorbidities such as cardiovascular diseases, blindness, kidney diseases, peripheral nerve damage, and erectile dysfunction.
- Survey respondents emphasized that dietary requirements, lifestyle modification, management of medications and side effects (weight gain) are associated with impaired work, travel and social life, increased stress, anxiety and financial burden.
- Treatments for type 2 diabetes are usually targeted toward glycemic control, though optimal blood glucose level is achieved by relatively few patients. However, it is patient perception that many current therapies fail to achieve glycemic control due to onset of adverse events such as hypoglycemia and significant weight gain.
- The majority of participants responded that maintaining satisfactory preprandial and postprandial glucose levels throughout the day as well as preventing hypoglycemia, change in weight, heart problems, gastrointestinal effects, and high blood pressure was important. Medications that are less costly, easy to administer and provide more energy, better mental health, and an overall sense of well-being while minimizing side effects were the preferred choice of treatments.
- Also important was avoiding the requirement for multiple antidiabetic therapies and diabetes-associated complications.

Clinical Trials

Five RCTs met the inclusion criteria of the systematic review conducted by CDR.

Placebo-Controlled Trials

Four double-blind, 24-week, placebo-controlled, phase III RCTs were included (GETGOAL – L [N = 496], GETGOAL – L Asia [N = 311], GETGOAL – DUO 1 [N = 446] and GETGOAL – L – C [N = 448]). All trials enrolled adult patients with type 2 diabetes mellitus with inadequate glycemic control on basal insulin therapy (alone or in combination with metformin) with the exception of GETGOAL – L Asia, which included patients with type 2 diabetes mellitus with inadequate glycemic control on basal insulin therapy (alone or in combination with sulfonylurea). The intervention in all placebo-controlled trials consisted of lixisenatide (initial dose 10 mcg titrated up to 20 mcg maintenance dose) in addition to permitted background therapy compared with placebo in addition to permitted background therapy). All placebo-controlled trials comprised a two-week screening phase, a one- to 12-week placebo run-in phase (to ensure optimal basal insulin titration), and a 24-week double-blind treatment phase followed by three days of follow-up.

Key limitations of the placebo-controlled trials include randomization potentially being compromised due to study withdrawals; concerns with the statistical testing across secondary end points; concerns with the imputation model and the definitions of intention-to-treat analysis and hypoglycemia; lack of control for multiple statistical testing across subgroups of interest and sensitivity analyses; large placebo response; and differences in patient and practice characteristics between the study centres included in the placebo-controlled trials and what would be seen in a Canadian setting (e.g., the mean age of patients, racial group, and use of optimal standard antidiabetic practices).

Active-Controlled Trial

One open-label, 26-week, active-controlled, phase III, noninferiority RCT was also included (GETGOAL – DUO 2 [N = 894]). The GETGOAL – DUO 2 study also enrolled adult patients with type 2 diabetes mellitus with inadequate glycemic control on basal insulin (insulin glargine) therapy (alone or in combination with metformin). The intervention consisted of lixisenatide (initial dose 10 mcg titrated up to 20 mcg maintenance dose) in addition to permitted background therapy compared with insulin glulisine once daily and insulin glulisine three times a day in addition to permitted background therapy. Subcutaneous insulin glulisine was administered within 15 minutes before breakfast or dinner in the group taking insulin glulisine once daily, and within 15 minutes before each meal in the group taking insulin glulisine three times a day. The initial insulin glulisine dose was three to five units per injection and subsequently titrated to obtain a self-monitored plasma glucose value between greater than 5.6 mmol/L and less than and equal to 7.8 mmol/L while avoiding hypoglycemia at every visit. GETGOAL – DUO 2 comprised a two-week screening phase, a 12-week run-in phase used to switch and optimize basal insulin (insulin glargine), and a 26-week open-label treatment phase followed by three days of follow-up.

Key limitations of the trial include its open-label design; concerns with the titration regimen of insulin (basal and prandial), imputation model, and definitions of intention-to-treat analysis and hypoglycemia; lack of per-protocol analysis for noninferiority tests; randomization potentially being compromised due to study withdrawals; lack of control for multiple statistical testing across all secondary end points, subgroups of interest and sensitivity analyses; concerns with the definitions of intent-to-treat analysis and hypoglycemia and the differences in patient and practice characteristics between the study centres included in GETGOAL – DUO 2 and what would be seen in a Canadian setting (e.g., the mean age of patients, racial group, and the use of optimal standard antidiabetic practices).

Outcomes

Outcomes were defined a priori in the CDR systematic review protocol. Of these, CDEC discussed the following:

- glycemic control (e.g., change in A1C, fasting plasma glucose, postprandial glucose)
- body weight (e.g., change in body weight)
- mortality
- change in insulin dose

- need for rescue therapy
- hospitalization
- health-related quality of life as assessed by the Impact of Weight on Quality of Life–Lite questionnaire
- adverse events, serious adverse events, withdrawals due to adverse events, notable harms (pancreatitis, anaphylaxis, hypoglycemia [including severe hypoglycemia]), and injection-site reactions and gastrointestinal adverse events (including nausea, diarrhea, and vomiting).

In the placebo-controlled trials, the primary efficacy outcomes were the absolute change from baseline in A1C at week 24. In the GETGOAL – DUO 2 study, the primary efficacy outcome was the absolute change from baseline in A1C at week 26.

Efficacy

Placebo-Controlled Trials

Patients treated with lixisenatide experienced a statistically significantly greater reduction in the primary end point of absolute change in A1C compared with placebo at week 24 in all placebo-controlled trials. The adjusted mean differences were –0.36% (95% confidence interval [CI], –0.55% to –0.17%), *P* = 0.0002; –0.88% (95% CI, –1.12% to –0.65%), *P* < 0.0001; –0.32% (95% CI, –0.46% to –0.17%), *P* < 0.0001; and –0.51% (95% CI, –0.69% to –0.34%), *P* < 0.0001 in GETGOAL – L, GETGOAL – L Asia, GETGOAL – DUO 1, and GETGOAL – L – C, respectively.

Patients treated with lixisenatide also experienced a statistically significantly greater reduction in two-hour postprandial glucose (adjusted mean differences were similar in all of the placebo-controlled trials: –3.81 mmol/L [95% CI, –4.70 to –2.93], *P* < 0.0001; −7.83 mmol/L [95% CI, –8.89 to –6.77], *P* < 0.0001; –3.16 mmol/L [95% CI, –3.95 to –2.38], *P* < 0.0001; and –3.45 mmol/L [95% CI, -4.23 to -2.67], *P* < 0.0001 in GETGOAL – L, GETGOAL – L Asia, GETGOAL – DUO 1, and GETGOAL – L – C, respectively) compared with placebo at week 24.

The adjusted mean differences between lixisenatide and placebo for the change in fasting plasma glucose were –0.08 mmol/L (95% CI, -0.59 to 0.43), *P* = 0.7579; –0.67 mmol/L (95% CI, –1.23 to –0.11); –0.12 mmol/L (95% CI, –0.46 to 0.23), *P* = 0.5142; and –0.38 mmol/L (95% CI, –0.79 to 0.02), *P* = 0.0650 in GETGOAL – L, GETGOAL – L Asia, GETGOAL – DUO 1 and GETGOAL – L – C, at week 24, respectively.

Patients treated with lixisenatide experienced a statistically significant reduction in body weight compared with patients allocated to placebo in both GETGOAL – DUO 1 and GETGOAL – L – C (adjusted mean differences were –0.89 kg [95% CI, –1.42 to –0.35], *P* = 0.0012 and –1.17 kg [95% CI, –1.60 to –0.74], *P* < 0.0001, respectively). No statistically significant differences in body weight were observed in GETGOAL – L Asia (adjusted mean difference was –0.43 kg [95% CI, –0.93 to 0.06], *P* = 0.0857). The adjusted mean difference between lixisenatide and placebo for the change in bodyweight was –1.28 kg (95% CI, –1.80 to –0.75) in GETGOAL – L.

The number of patients needing rescue therapy in the placebo groups compared with the lixisenatide groups in GETGOAL – L, GETGOAL – L Asia, and GETGOAL – DUO 1 were 7%, 3%, and less than 1% compared with 6%, 1%, and less than 1%, respectively. No data were provided for the need for rescue therapy in GETGOAL – L – C.

Patients treated with lixisenatide required statistically significantly less total daily basal insulin compared with patients allocated to placebo at week 24 in GETGOAL – DUO 1 and GETGOAL – L - C (adjusted mean differences were –2.24 units per day [95% CI, −4.26 to –0.22], *P* = 0.0300, and –1.11 units per day [95% CI, –1.86 to –0.37], *P* = 0.0033, respectively). The adjusted mean differences for the change in total daily basal insulin in GETGOAL – L and GETGOAL – L Asia at week 24 were –3.69 units per day (95% CI, –6.57 to –0.82) and –1.29 units per day (95% CI, –2.10 to –0.48), respectively.

Active-Controlled Trial

Patients treated with lixisenatide and insulin glulisine experienced numerical reductions in A1C at week 26 compared with patients treated with insulin glulisine once daily and insulin glulisine three times a day (adjusted mean differences were –0.05% [95% CI, −0.17% to 0.06%] and 0.21% [95% CI, 0.1% to 0.33%], respectively). Based on the adjusted mean differences and the pre-specified

noninferiority margin for change in A1C (0.4%), lixisenatide was statistically noninferior to both insulin glulisine once daily and insulin glulisine three times a day in terms of the primary end point of absolute change from baseline in A1C at week 26.

The adjusted mean difference between lixisenatide and insulin glulisine once daily or insulin glulisine three times a day for the change in two-hour postprandial glucose and fasting plasma glucose were –2.07 mmol/L (95% CI, –3.29 to –0.85) and –2.23 mmol/L (95% CI, –3.39 to –1.07), and –0.01 mmol/L (95% CI, –0.32 to 0.30) and –0.17 mmol/L (95% CI, –0.48 to 0.143) at week 26, respectively.

Patients treated with lixisenatide experienced a reduction in body weight whereas both patients in the group taking insulin glulisine once daily and patients in the group taking insulin glulisine three times a day experienced an increase in body weight at week 26. The adjusted mean differences were similar in both insulin glulisine once daily and insulin glulisine three times a day treatment groups and were statistically significantly in favour of lixisenatide (–1.66 kg [95% CI, –2.26 to –1.06] and –1.99 kg [95% CI, –2.59 to −1.40], respectively). Lixisenatide was found to be superior to insulin glulisine three times a day in the co-primary end point of change in body weight at week 26. The adjusted mean differences for the change in total daily basal insulin between lixisenatide and insulin glulisine once daily and insulin glulisine three times a day were 0.76 units per day (95% CI, −1.41 to 2.92) and 3.83 units per day (95% CI, 1.66 to 6.00), respectively.

Mean total daily insulin glulisine doses were [redacted] compared with 9.97 units per day and 20.24 units per day in the insulin glulisine once daily and insulin glulisine three times a day groups, respectively, [redacted] and week 26. Mean total daily insulin doses [redacted] compared with 73.61 units per day and 81.05 units per day in the insulin glulisine once daily and insulin glulisine three times a day groups, respectively, [redacted] and week 26.

[redacted]

Harms (Safety and Tolerability)

Placebo-Controlled Trials

In the placebo-controlled trials, treatment-emergent adverse events ranged between 64% and 89% in the lixisenatide groups versus 41% and 86% in the placebo groups. The most commonly reported adverse events that occurred more frequently in the lixisenatide treatment groups compared with the placebo groups were hypoglycemia (ranged between 25% and 44% compared with 19% and 41%, respectively), nausea (ranged between 23% and 40% compared with 5% and 10%, respectively), headache (ranged between 2% and 13% compared with 0% and 10%, respectively), diarrhea (ranged between 3% and 11% compared with 2% and 6%, respectively), vomiting (ranged between 9% and 18% compared with 1% and 2%, respectively), and decreased appetite (ranged between 2% and 7% compared with 0% and 1%, respectively).

Serious adverse events were reported more frequently in the lixisenatide group compared with the placebo group (5% to 14% compared with 1% to 10%, respectively), with a similar frequency across all placebo-controlled trials.

The proportion of patients in the lixisenatide group who withdrew due to adverse events compared with the placebo group in all placebo-controlled trials ranged between 4% and 11% versus 2% and 7%, respectively. The most commonly reported adverse events leading to withdrawals that occurred more frequently in the lixisenatide treatment groups compared with the placebo groups were hypoglycemia, nausea, and vomiting. Overall, the frequency of withdrawals due to adverse events was relatively similar across trials.

A total of [redacted], one death in GETGOAL – L Asia, and two deaths in GETGOAL – DUO 1; however, none of the deaths were considered to be related to study treatment by the investigators and adjudication committee. No deaths were reported in GETGOAL – L – C.

For some of the notable harms — specifically hypoglycemia, nausea, diarrhea, and vomiting — a numerically greater percentage of patients experienced an event in the lixisenatide group compared with the placebo group in all the placebo-controlled trials: hypoglycemia (42% versus 41%, 44% versus 24%, 27% versus 19%, and 25% versus 20% for the lixisenatide versus the placebo groups in GETGOAL – L, GETGOAL – L Asia, GETGOAL – DUO 1, and GETGOAL – L – C, respectively), nausea (29% versus 10%, 40% versus 5%, 27% versus 5%, and 23% versus 5% for the lixisenatide versus the placebo groups in GETGOAL – L, GETGOAL – L Asia, GETGOAL – DUO 1, and GETGOAL – L – C, respectively), diarrhea (11% versus 6%, 7% versus 3%, 7% versus 3%, and [redacted] for the lixisenatide versus the placebo groups in GETGOAL – L, GETGOAL – L Asia, GETGOAL – DUO 1, and GETGOAL – L – C, respectively), vomiting (10% versus 1%, 18% versus 2%, 9% versus 1%, and 11% versus 1% for the lixisenatide versus the placebo groups in GETGOAL – L, GETGOAL – L Asia, GETGOAL – DUO 1, and GETGOAL – L – C, respectively). The occurrence of the remaining notable harms — specifically allergic reaction, pancreatitis, injection-site reaction, and severe hypoglycemia — was approximately equal in both treatment groups across all the placebo-controlled trials, with the exception of injection-site reaction in GETGOAL – DUO 1 (7% in the lixisenatide group compared with 2% in the placebo group).

Active-Controlled Trial

In GETGOAL – DUO 2, 74% of patients experienced treatment-emergent adverse events versus 74% and 80% in the insulin glulisine once daily and insulin glulisine three times a day groups, respectively. The most commonly reported adverse events that occurred more frequently in the lixisenatide treatment group compared with the insulin glulisine once daily and insulin glulisine three times a day groups were nausea (25% versus 2% and 1%, respectively), diarrhea (7% versus 3% and 1%, respectively), and vomiting (9% versus 2% and 2%, respectively). Contrarily, one commonly reported adverse event occurred more frequently in the insulin glulisine once daily and insulin glulisine three times a day groups compared with the lixisenatide group: hypoglycemia (47% and 52% versus 36%, respectively).

Serious adverse events were reported by 4% to 5% of patients, with a similar frequency between all treatment groups.

The proportion of patients in the lixisenatide group that withdrew due to adverse events compared with the insulin glulisine once daily and insulin glulisine three times a day groups were 5% versus 1% and 1%, respectively. The most commonly reported adverse events leading to withdrawal that occurred more frequently in the lixisenatide treatment groups compared with the insulin glulisine once daily and insulin glulisine three times a day groups were nausea and vomiting.

A total of three deaths occurred in GETGOAL – DUO 2; however, none of the deaths were considered to be related to study treatment by the investigators and adjudication committee.

For some of the notable harms — specifically nausea, diarrhea, and vomiting — a numerically greater percentage of patients experienced an event in the lixisenatide group compared with the insulin glulisine once daily and insulin glulisine three times a day groups: nausea (25% versus 2% and 1%, respectively), diarrhea (7% versus 3% and 1%, respectively), and vomiting (9% versus 2% and 2%, respectively). Contrarily, one commonly reported adverse event occurred more frequently in the insulin glulisine once daily and insulin glulisine three times a day groups compared with the lixisenatide group: hypoglycemia (47% and 52% versus 36%, respectively). Occurrences of the remaining notable harms — specifically allergic reaction, pancreatitis, injection-site reaction, and severe hypoglycemia — were approximately equal in all treatment groups.

Cost and Cost-Effectiveness

At the submitted price of $56.98 per 0.05 mg/mL or 0.1 mg/mL pre-filled pen, lixisenatide ($4.07 daily) is less expensive than liraglutide 1.2 mg daily ($4.57), liraglutide 1.8 mg ($6.85), exenatide (Byetta) 5 mcg or 10 mcg twice daily ($4.79), exenatide (Bydureon) 2 mg weekly ($6.92 daily), and dulaglutide 0.75 mg to 1.5 mg weekly ($6.01 daily). The annual cost of lixisenatide is $1,486.

The manufacturer submitted a cost-utility analysis comparing lixisenatide with prandial insulin in patients with type 2 diabetes mellitus failing to reach optimal glycemic control despite being treated with basal insulin (with or without metformin) over a lifetime time horizon (25 years) from the perspective of the Canadian health care payer. The economic model was based on the United Kingdom Prospective Diabetes Study Outcomes Model and was informed by patient data from the United Kingdom Prospective Diabetes Study and the GETGOAL – DUO 2 study. The treatment effects and safety (adverse events) of basal plus lixisenatide and basal plus

prandial (bolus) were taken from the GETGOAL – DUO 2 trial. Other inputs such as costs and utility values were obtained from published literature. The manufacturer reported that lixisenatide dominated (i.e., was more effective and less costly than) prandial insulin, with a cost savings of $8,331 and incremental quality-adjusted life-years (QALYs) of 0.0793.

CDR identified the following key limitations with the manufacturer's economic submission:

- Surrogate outcomes of hemoglobin A1C and body mass index from the GETGOAL – DUO 2 trial were used to predict long-term microvascular and macrovascular complications.
- The relative efficacy and safety (hypoglycemia) were determined from a trial in patients naive to both prandial insulin and lixisenatide. It is unclear if the relative efficacy and safety in a prandial-naive population observed over 26 weeks in this patient population persists over a lifetime.
- The dose of prandial insulin examined in GETGOAL – DUO 2 is much lower than the dose used in the model; the dose used in the model was taken from cross-sectional data that would include patients experienced on insulin. The model assumes efficacy and harms from the GETGOAL – DUO 2 study (prandial naive) but uses doses from observational data (prandial experienced), which is not appropriate, and favours lixisenatide.
- The lowest cost regular human insulin (recommended by CADTH) was not used in the base case.

In a plausible CDR base case, an average prandial insulin dose of 40 international units and using lowest cost of human insulin was used. The incremental cost-utility ratio (ICUR) for lixisenatide was $63,818 per QALY when compared with prandial insulin. In a scenario analysis, using alternate values for disutility of hypoglycemia, the ICUR increased to more than $100,000 per QALY when compared with prandial insulin. Additional scenario analyses on the CDR base case were undertaken considering the average daily prandial dose from the trial (20.24 international units), which increased the ICUR to $112,093 per QALY.

A series of price-reduction analyses undertaken based on the CDR base case and scenario analyses of the CDR base case indicate that a price reduction of 6% to 19% may be required to achieve an ICUR, compared with prandial insulin, below $50,000 per QALY.

CADTH Canadian Drug Expert Committee Members:

Dr. James Silvius (Chair), Dr. Silvia Alessi-Severini, Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Dr. Peter Jamieson, Dr. Anatoly Langer, Mr. Allen Lefebvre, Dr. Kerry Mansell, Dr. Yvonne Shevchuk, and Dr. Adil Virani.

October 18, 2017

Regrets:

None

Conflicts of Interest:

None