CADTH Proposed Project Scope

Utilization Analysis of Glucagon-Like Peptide 1 Agonists

Date: May 9, 2022

For stakeholder feedback

Background and Rationale

Glucagon-like peptide 1 (GLP-1) receptor agonists have been approved in Canada for the improvement of glycemic control in adult patients with type 2 diabetes (T2DM), either as an adjunct therapy to diet and exercise or in combination with other antidiabetic drugs in addition to diet and exercise (**Table 1**).[1-7] Two of these GLP-1s (liraglutide and semaglutide) also have brand name versions approved for weight management.[8,9]

Table 1. GLP-1 Products Approved in Canada

Generic name (Brand name)	Manufacturer	Health Canada-approved indication:
Dulaglutide (Trulicity)	Eli Lilly Canada Inc.	Adults with T2DM, in combination with: • diet and exercise in patients for whom metformin (MET) is inappropriate due to contraindication or intolerance. • MET, when diet and exercise plus maximal tolerated dose of MET do not achieve adequate glycemic control. • MET and a sulfonylurea (SU), when diet and exercise plus dual therapy with MET and a SU do not achieve adequate glycemic control. • sodium glucose co-transporter 2 inhibitor (SGLT2i) with MET, when diet and exercise plus SGLT2i with or without MET do not achieve adequate glycemic control. • basal insulin with MET, when diet and exercise plus basal insulin with or without MET do not achieve adequate glycemic control. • prandial insulin with MET, when diet and exercise plus basal or basal-bolus insulin therapy (up to two injections of basal or basal plus prandial insulin per day) with or without oral antihyperglycemic medications, do not achieve adequate glycemic control.
Exenatide (Byetta; Bydureon)	AstraZeneca Canada Inc.	**Byetta** Adults with T2DM, in combination with: • MET and/or a SU, when maximally tolerated doses of these oral therapies in addition to diet and exercise do not provide adequate glycemic control. • insulin glargine (with or without MET) when insulin glargine (with or without MET), in addition to diet and exercise, does not provide adequate glycemic control.
		Bydureon Adults with T2DM, in combination with:

		• diet and exercise for whom MET is inappropriate due to contraindications or intolerance. • MET when MET used alone, with diet and exercise, does not provide adequate glycemic control. • a SU when the SU used alone, with diet and exercise, does not provide adequate glycemic control. • MET and a SU when dual therapy with these two agents, with diet and exercise, does not provide adequate glycemic control. • basal insulin (alone or with MET) when therapy with these agents, with diet and exercise, does not provide adequate glycemic control.
Liraglutide (Victoza; Saxenda)	Novo Nordisk Canada Inc.	**Victoza** Adults with T2DM, in combination with: • diet and exercise in patients for whom MET is inappropriate due to contraindication or intolerance. • MET, when diet and exercise plus maximal tolerated dose of MET do not achieve adequate glycemic control. • MET and a SU, when diet and exercise plus dual therapy with MET and a SU do not achieve adequate glycemic control. • MET and a SGLT2i, when diet and exercise plus dual therapy with MET and a SGLT2i do not achieve adequate glycemic control. • MET and basal insulin, when diet and exercise plus dual therapy with Victoza® and MET do not achieve adequate glycemic control.
		Saxenda As an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of: • 30 kg/m^2 or greater (obesity), or • 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbidity (e.g., hypertension, T2DM, or dyslipidemia) and who have failed a previous weight management intervention.
Lixisenatide (Adlyxine)	Sanofi-aventis Canada Inc.	Adults with T2DM, as an adjunct to diet and exercise, in combination with: • metformin • a SU (alone or with MET) • pioglitazone (alone or with MET) • a basal insulin (alone or with MET)

Semaglutide (Ozempic; Rybelsus; Wegovy)	Novo Nordisk Canada Inc.	**Ozempic** Adults with T2DM, in combination with: • diet and exercise in patients for whom MET is inappropriate due to contraindication or intolerance. • MET, when diet and exercise plus maximal tolerated dose of MET do not achieve adequate glycemic control. • MET and a SU, when diet and exercise plus dual therapy with MET and a SU do not achieve adequate glycemic control. • MET or a SU and a SGLT2i, when diet and exercise plus MET or a SU, in addition to an SGLT2i, do not achieve adequate glycemic control. • basal insulin with MET, when diet and exercise plus basal insulin with MET do not achieve adequate glycemic control.
		Rybelsus Adults with T2DM, in combination with: • diet and exercise in patients for whom MET is inappropriate due to contraindication or intolerance. • other medicinal products for the treatment of diabetes.
		Wegovy As an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients with an initial BMI of: • 30 kg/m^2 or greater (obesity), or • 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, T2DM, dyslipidemia, or obstructive sleep apnea.

All GLP-1 formulations are administered via subcutaneous (SC) injection except one oral formulation of semaglutide (Rybelsus). The Canadian Drug Expert Committee (CDEC) recommendations for dulaglutide (Trulicity), lixisenatide (Adlyxine), SC semaglutide (Ozempic), and oral semaglutide (Rybelsus) were issued in June 2016, November 2017, May 2019, and June 2021, respectively, and these drugs all received a recommendation to "reimburse with clinical criteria and/or conditions" for adults with T2DM (**Table 2**).[10-13] CDEC recommendations for exenatide (Byetta) and liraglutide (Victoza) were issued in July 2012 and September 2011, respectively, and these drugs received a "do not list" recommendation.[14,15] The extended-release version of exenatide (Bydureon) has not been reviewed by CDEC.

Table 2. Conditions for reimbursement (according to CDEC) of GLP-1s for adults with T2DM

Generic name	Brand name	Conditions for reimbursement
Dulaglutide	Trulicity	Must be used in combination with MET alone or with MET and a SU.
Lixisenatide	Adlyxine	Must be used in combination with basal insulin alone or with MET and basal insulin.
Semaglutide	Ozempic	Must be used in combination with MET alone.
	Rybelsus	Must be used in combination with MET alone or with other antihyperglycemic agents except another GLP-1 or dipeptidyl peptidase 4 (DPP-4) inhibitors.

More recently, due to their additional effects on weight reduction and approval for weight management (for liraglutide and SC semaglutide),[8,9,16-18] GLP-1s have now been submitted for CDEC review for this indication (**Table 3**).[19,20]. Saxenda received a "do not reimburse" recommendation from CDEC in September 2021.[19] Wegovy was submitted for CDEC review in March 2022 and is expected to be reviewed during the July 2022 CDEC meeting.[20]

Table 3. Dosing for GLP-1s (administered subcutaneously) indicated for both T2DM and weight management

Generic name	Brand name	Dosing information
Liraglutide	Victoza	**Starting dose**: 0.6 mg daily **Maintenance dose:** escalate to a maintenance dose of 1.8 mg daily starting at week 3
	Saxenda	**Starting dose**: 0.6 mg daily **Maintenance dose:** escalate to a maintenance dose of 3.0 mg daily at week 5
Semaglutide	Ozempic	**Starting dose**: 0.25 mg weekly **Maintenance dose (at initial approval):** escalate to a maintenance dose of 1.0 mg weekly at week 5 **Maintenance dose (as of January 2022):** escalate to a maintenance dose of 2.0 mg weekly at week 5
	Wegovy	**Starting dose**: 0.25 mg weekly **Maintenance dose:** escalate to a maintenance dose of 2.4 mg weekly at week 17

Policy Issue

Given the prevalence of obesity in Canada (~1/4 adults),[21] the use of GLP-1s for weight management will have a significant impact on the utilization of and expenditures on these drugs in this country. Currently, reimbursement of a GLP-1 in Canada is only for patients with T2DM and conditional on their use as part of an antidiabetic regimen involving combination pharmacological therapy. As weight loss is a class effect associated with GLP-1s[18] and with the T2DM formulations of these drugs already on the Canadian market, it is possible that physicians may already be prescribing these medications to patients for weight management (i.e., off-label). More specifically, lixisenatide (Adlyxine) and semaglutide (Ozempic) are listed as an open benefit on some public drug plan formularies (e.g., Ontario and NIHB).[22] In light of these factors, there is a need to understand the current utilization of GLP-1s across Canada and ensure their appropriate use.

Research Questions

1. What are the current utilization and dosing patterns (for liraglutide and semaglutide only) of GLP-1s nationally and within each jurisdiction?
2. What proportion of patients prescribed a GLP-1 are using it for weight management versus for T2DM?
    a) Have patients prescribed a GLP-1 had a prior claim for another antidiabetic drug or glucose monitoring device (i.e., glucometer with strips, flash glucose monitoring, or continuous glucose monitoring)?
    b) Are patients prescribed a GLP-1 using it in combination with other antidiabetics drugs and, if so, what specific combination regimens are being utilized?

Project Description

The project with be a utilization analysis using drug claims data from the National Prescription Drug Utilization Information System (NPDUIS). The analysis will assess market share, dosing (for liraglutide and semaglutide only), drug expenditures, and prior and concurrent antidiabetic drug use (**Table 4**).

Table 4. Project Scope

Criteria	Description
Population	Adults prescribed a GLP-1 indicated for T2DM
Interventions	GLP-1s approved for the treatment adults with T2DM in Canada (i.e., dulaglutide, exenatide, liraglutide, lixisenatide, and semaglutide)
Outcomes	Market share, dosing (for semaglutide and liraglutide only), expenditures, and prior and concurrent antidiabetic drug use

Key Project and Protocol Components

To address the research questions, this utilization analysis will include the following key components:

- NPDUIS data on the market share, dosing (for liraglutide and semaglutide only), and expenditures on GLP-1s nationally and within jurisdictions.
- Drug claims prior to GLP-1 use
- Drug claims in concurrence with GLP-1 use

Status of the Document

This proposed project scope will be posted for 10 business days as of the date of this posting (May 30, 2022) for stakeholder feedback. The feedback will be considered as the project plan finalized.

References

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4. Novo Nordisk Canada Inc. Victoza® Product Monograph. 2020.
5. Novo Nordisk Canada Inc. RYBELSUS® Product Monograph. 2020.
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9. Novo Nordisk Canada Inc. SAXENDA® Product Monograph. 2021.
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11. CADTH. Semaglutide (Ozempic) - Reimbursement Review.
12. CADTH. Dulaglutide (Trulicity) - Reimbursement Review.
13. CADTH. Semaglutide (Rybelsus) - Reimbursement Review.
14. CADTH. Liraglutide (Victoza) - Reimbursement Review.
15. CADTH. Exenatide (Byetta) - Reimbursement Review.
16. Davies MJ, Bergenstal R, Bode B, et al. Efficacy of Liraglutide for Weight Loss Among Patients With Type 2 Diabetes: The SCALE Diabetes Randomized Clinical Trial. *JAMA.* 2015;314(7):687-699.
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20. CADTH. Semaglutide (Wegovy) - Reimbursement Review.
21. Statistics Canada. Health Fact Sheets - Overweight and obese adults, 2018.
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