CADTH

CADTH IMPLEMENTATION ADVICE

Freestyle Libre Flash Glucose Monitoring System

(ABBOTT LABORATORIES CO.)

INDICATION: Measurement of interstitial fluid glucose levels in adults aged 18 years and older

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CADTH

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Abbreviations

A1C	glycated hemoglobin
CGM	continuous glucose monitoring
CSEMI	Comité scientifique de l'évaluation des médicaments aux fins d'inscription / Standing Scientific Committee on Entry on the List of Medications
FGMS	flash glucose monitoring system
HQO	Health Quality Ontario
HTA	health technology assessment
IIT	intensive insulin therapy
INESSS	Institut national d'excellence en santé et en services sociaux
OHTAC	Ontario Health Technology Advisory Committee
RCT	randomized clinical trial
RAMQ	Régie de l'assurance maladie du Québec
SMBG	self-monitoring of blood glucose
T1D	type 1 diabetes
T2D	type 2 diabetes

Product	Freestyle Libre Flash Glucose Monitoring System
Indication	Measurement of interstitial fluid glucose levels in adults aged 18 years and older
Manufacturer	Abbott Laboratories Co.

Background and Policy Issue

Given the increasing demand from patients and health care professionals to have publicly funded access to Freestyle Libre Flash Glucose Monitoring System (FGMS), public drug plans in Canada are seeking guidance for policy decisions. CADTH therefore initiated a project to inform jurisdictional decision-making on funding of this technology. The initial phase of this project was to synthesize results from two publicly available recent Canadian health technology assessments (HTAs) on Freestyle Libre FGMS (Abbott Laboratories Co.) by Health Quality Ontario (HQO)[1] and the Institut national d'excellence en santé et services sociaux (INESSS).[2] Findings from these two HTAs, along with the associated funding recommendations from HQO (under the guidance of the Ontario Health Technology Advisory Committee [OHTAC])[3] as well as from INESSS and the Comité scientifique de l'évaluation des médicaments aux fins d'inscription/Standing Scientific Committee on Entry on the List of Medications (CSEMI)[4,5], were summarized in a CADTH Technology Review report. A draft version of the latter was posted between May 21 and June 4, 2020 on the CADTH website to solicit feedback from stakeholders, including patients and their representatives, caregivers, clinicians, and other stakeholders such as advocacy groups and pharmaceutical manufacturers. The Technology Review report was subsequently revised to account for feedback received.

The second phase of this project consisted of CADTH convening an implementation advice panel (IAP). This panel was tasked to further contextualize the information contained in the Technology Review report and identify additional considerations such as specific groups of patients who may particularly benefit from using FGMS and determine the key benefits of using this technology. This consultation aimed to develop an advice for Canadian public drug plans regarding the potential implementation of the two currently available provincial funding recommendations for Freestyle Libre FGMS.

Policy Questions

Two policy questions were identified for this project:

- Is there a group of patients with diabetes that may particularly benefit from using Freestyle Libre FGMS versus using a more traditional glycemia monitoring method such as test strips?
- If so, what criteria should be used to identify the patients for whom Freestyle Libre FGMS could be reimbursed by the public drug programs?

Consultation Process and Objectives

The objective of this project was to develop implementation advice that would inform public funding of Freestyle Libre FGMS in Canada; an IAP was convened by CADTH for that purpose. This panel was composed of four experts, three endocrinologists and one nurse manager working in a regional health authority in Canada; some IAP members had experience with the HTA process. Therefore, the IAP members had collective experience in the clinical management of diabetes, management of health care resources, and development of health policies. They shared their expertise to help develop the advice on the implementation of the Freestyle Libre FGMS funding recommendations recently released by HQO/OHTAC and INESSS/CSEMI.

The advice developed by the IAP does not constitute an evidence-based recommendation; rather, it is evidence-informed implementation advice, based on two recent Canadian HTAs and provincial funding recommendations on FGMS. This advice is being provided to publicly funded drug plans to assist with decision-making regarding the reimbursement of Freestyle Libre FGMS in Canada.

Members of the IAP provided initial input using a questionnaire that was developed by CADTH and representatives of the public drug programs (Appendix 1). This questionnaire included three questions designed to gain insight into the following considerations:

- what population(s) are likely to benefit the most from using Freestyle Libre FGMS?
- what testing methods are these patients currently using to monitor their glycemia?
- what are the anticipated improved outcomes of using Freestyle Libre FGMS for the population(s) expected to benefit the most from using this technology?

The questionnaire was distributed to the experts before the IAP meeting, along with a draft version of the CADTH Technology Review report on FGMS. Panellists were asked to consider the evidence and the recommendations included in the draft CADTH Technology Review report when responding to the questionnaire. A summary of the expert input was prepared by CADTH to identify the most frequently cited or important elements of the responses received. This summary was shared with IAP members in advance of the teleconference panel meeting hosted by CADTH. Using the summary of feedback provided, the panellists attempted to reach consensus on the most important patient characteristics, most relevant comparators, as well as the anticipated improved outcomes of using Freestyle Libre FGMS. CADTH drafted the Implementation Advice report based on the panel discussion.

A draft version of this Implementation Advice report was posted between July 13 and July 27, 2020 on the CADTH website to solicit feedback from stakeholders, including patients and their representatives, caregivers, clinicians, and other stakeholders such as advocacy groups and pharmaceutical manufacturers. The Implementation Advice report was subsequently revised to account for feedback received.

Implementation Advice

Provincial Funding Recommendations for FGMS

The two Freestyle Libre FGMS provincial funding recommendations relevant to this report were respectively developed by HQO/OHTAC and INESSS/CSEMI.

HQO/OHTAC

Based on the guidance of OHTAC, HQO recommended publicly funding FGMS for the following two groups of patients:

- persons with type 1 diabetes (T1D) who experience recurrent hypoglycemia despite frequent self-monitoring of blood glucose (SMBG) and efforts to optimize insulin management
- persons with type 2 diabetes (T2D) requiring intensive insulin therapy (IIT); that is, multiple daily injections of insulin or continuous subcutaneous insulin infusion for those who experience recurrent hypoglycemia despite frequent SMBG and efforts to optimize insulin management.[3]

The Ontario Drug Benefit Program started to reimburse FreeStyle Libre on September 16, 2019 for persons using insulin. Patients residing in Ontario are eligible to have 33 sensors reimbursed each year provided they have a valid prescription from a physician or nurse practitioner.[6]

INESSS/CSEMI

In October 2018, INESSS evaluated Freestyle Libre FGMS.[4] At that time, CSEMI recommended to add Freestyle Libre to the list of the prescription drug insurance plan for self-monitoring of glycemia in patients on insulin therapy, provided the economic burden is lessened. If the economic burden of funding Freestyle Libre was not reduced for the province, CSEMI recommended that this FGMS be listed as an exceptional drug product for adults aged 18 years and older who have at least two years of experience in self-managing their diabetes and who meet the following three criteria:

- IIT
- frequent or severe hypoglycemia events
- necessity for blood glucose self-monitoring at least eight times daily.[4,7]

Freestyle Libre FGMS has been reimbursed in Quebec since July 2019; the Régie de l'assurance maladie du Québec
(RAMQ) authorization form must be completed by the attending physician.[8] INESSS also added an implementation-related consideration to its recommendation; that is, training so that patients can master sensor application and learn how to interpret and use the information provided by the device. More specifically, the initial request is authorized for three months to evaluate patient capacity to use Freestyle Libre FGMS and wear the sensor. Request to pursue treatment is authorized for maximum of twelve months if patients show a capacity to make an optimal use of Freestyle Libre FGMS; that is at least 70% of the time.[4]

The recommendation from CSEMI was updated in April 2020 based on a change to the Health Canada labelling of August 2019, which no longer requires that patients have at least two years of experience in diabetes self-management.[5] The most recent funding recommendations therefore applies to persons with diabetes who are at least 18 years of age who meet the following three criteria:

- IIT (i.e., use of insulin pump therapy or three or more insulin injections per day)
- frequent or severe hypoglycemic events
- necessity for blood glucose self-monitoring at least eight times daily.[5]

The initial request is now authorized for six months (instead of three) to evaluate patient capacity to use Freestyle Libre FGMS and wear the sensor. Requests to pursue treatment are still authorized for twelve months if patients show a capacity to optimally use Freestyle Libre FGMS (that is, at least 70% of the time).[5] This assessment is done by the treating physician who must complete the Freestyle Libre Authorization Form when seeking reimbursement of this device for his/her patients.[9] The updated coverage criteria were implemented by RAMQ on April 29, 2020.[10]

Implementation Issues

The implementation advice from the panel is summarized in Table 1. For each issue, a summary of the relevant panel meeting discussion is provided below for additional context. The scope of this implementation advice is based on both the HQO and INESSS funding recommendations.

Table 1: Summary of Advice for Addressing Implementation Issues

Issue	Advice

Implementation issue 1: population(s) expected to benefit most from using Freestyle Libre FGMS	Among patients with insulin-treated diabetes, certain subgroups may be expected to benefit from using FGMS. These would include:
	• adults and children (with either T1D or T2D) on IIT[a] as part of a strategy to achieve individualized glycemic targets, and/or;
	• patients with certain conditions or special needs including, but not limited to those:
	  ○ adults and children:
	  ▪ on IIT[a] with highly labile glycemia[b] despite optimized diabetes care[c], or
	  ▪ with T1D requiring IIT[a] having hypoglycemia unawareness[d] and/or frequent hypoglycemic episodes[e] who do not have access to CGM, or
	  ▪ using insulin therapy who cannot perform finger pricking as part of SMBG because of certain barriers such as impaired dexterity or mobility, dermatological problems, occupational limitations, or other similar reasons.[f]
	  ○ women with T1D who are pregnant or planning a pregnancy within the next 12 months and who do not have access to real-time CGM.

Implementation issue 2: current alternative glycemic testing methods	The alternative glycemic testing method is SMBG, which involves the use of test strips and lancets to prick fingertips.
Implementation issue 3: anticipated improved outcomes of using Freestyle Libre FGMS for the population(s) expected to benefit the most from using this technology	While the HTAs found limited scientific evidence of reduced frequency and duration of hypoglycemia in adults with T1D and in adults with T2D using IIT[a], as well as improved time spent in target glycemic range in adults with T1D, IAP members clarified that the main outcome change of using FGMS is to improve hypoglycemia events. Other clinically relevant benefits of using FGMS, compared with using SMBG, are enhanced patient comfort, convenience, and independence as well as improved patient compliance in testing and better

Issue	Advice
	disease management due to availability of multiple, frequent data points for the analysis of glycemic trends.

[a] IIT requires patients to use basal bolus insulin therapy.

[b] Highly labile glycemia refers to a glycemic profile that tends to often swing between hypoglycemia and hyperglycemia despite patients regularly monitoring their glycemia.

[c] Optimized diabetes care refers to a situation where the physician/health care provider has tried to adjust all aspects of therapy he/she was capable of.

[d] The HQO report excluded people with hypoglycemic unawareness who are at high risk for glycemic variability stating that CGM, with alerts to prevent high or low blood glucose levels, would be more suitable for these people.[1]

[e] Frequent hypoglycemic episodes refer to a frequency and degree of hypoglycemia that impact a person's daily functioning.

[f] Barriers to using SMBG (with test strips and lancets) are best assessed by the health care provider/physician caring for the patient. Drug plans may consider implementing a special authorization form for these circumstances where the other criteria do not apply.

CGM = continuous glycemic monitoring; FGMS = flash glucose monitoring system; HTA = health technology assessment, IAP = implementation advice panel; IIT = intensive insulin therapy; SMBG = self-monitoring of blood glucose; T1D = type 1 diabetes; T2D = type 2 diabetes.

Implementation Issue 1 (population[s] expected to benefit most from using FGMS)

Among patients with insulin-treated diabetes, certain subgroups may be expected to benefit from using Freestyle Libre FGMS. These would include:

- adults and children (with either T1D or T2D) on IIT as part of a strategy to achieve individualized glycemic targets and/or;
- patients with certain conditions or special needs including, but not limited to, those:
  - adults and children:
    - on IIT with highly labile glycemia despite optimized diabetes care, or;
    - with T1D requiring IIT with hypoglycemia unawareness and/or frequent hypoglycemic episodes who do not have access to real-time continuous glycemic monitoring (CGM), or;
    - using insulin therapy who cannot perform finger pricking as part of SMBG because of certain barriers such as impaired dexterity or mobility, dermatological problems, occupational limitations, or other similar reasons.
  - women with T1D who are pregnant or planning a pregnancy within the next 12 months and who do not have access to real-time CGM.

In addition, during the consultation, IAP members:

- indicated that patients with T1D requiring IIT may potentially derive a greater benefit; that is a reduction in hypoglycemia, from using FGMS; patients with T2D requiring similar therapy would nonetheless also be expected to have improved hypoglycemia with this technology
- indicated that patients requiring IIT due to other causes (e.g., pancreatogenic diabetes [including diabetes resulting from chronic pancreatitis] — this condition is sometime referred to type 3c diabetes) — may also benefit from using FGMS
- acknowledged that there could be potential for significant budgetary impact to public drug plans in funding FGMS. Consequently, when developing reimbursement criteria for FGMS, consideration may be given to combining key clinical characteristics that patients should present in order to access this technology. For example, it was noted that patients who are unable to perform multiple daily glycemic tests and record associated results (for a variety of reasons, including access, professional occupation or lifestyle), may particularly benefit from using FGMS. Accordingly, a potential subgroup of patients

presenting with several clinical features that may be considered for reimbursement of FGMS would be composed of individuals with either T1D or T2D, requiring IIT, and who are unable to do multiple daily glycemic tests.

The panel further indicated that not all patients with diabetes are expected to benefit from using FGMS. There is no evidence to indicate that patients not using insulin benefit from using this technology. However, among patients with insulin-treated diabetes, certain subgroups may be expected to benefit from using Freestyle Libre FGMS; these were described in the preceding paragraphs. Also, IAP members clarified that evidence was not available in the HTAs reviewed for all subgroups identified above; as such some of these statements are based on their expert opinion. Lastly, in the context of this implementation advice, IAP members further clarified that:

- IIT refers to the use of basal bolus insulin therapy
- highly labile glycemia refers to a glycemic profile that tends to often swing between hypoglycemia and hyperglycemia despite patients regularly monitoring their glycemia
- optimized diabetes care refers to a situation where the physician/health care provider has tried to adjust all aspects of therapy he/she was capable of
- frequent hypoglycemic episodes refer to a frequency and degree of hypoglycemia that impact a person's daily functioning
- barriers to using SMGB (with test strips and lancets) are best assessed by the physician/health care provider caring for the patient. Drug plans may consider implementing a special authorization form for these circumstances where the other criteria do not apply.

Implementation Issue 2 (current alternative glycemic testing methods)

In the populations identified above, patients are currently managed with SMBG which involves use of test strips and lancets to prick fingertips. Accordingly, IAP members deemed this traditional approach of monitoring glycemia to be the current alternative to Freestyle Libre FGMS. Compared to SMBG, IAP members specified that Freestyle Libre FGMS provides the ability to analyze glycemic trends to support better disease management. While the flash sensor does not require finger prick calibration with SMBG, both the HQO and the INESSS HTA reports acknowledge that occasional finger prick testing — with test strips — may be indicated for patients using FGMS. These are done to ensure accuracy of glycemic readings in certain situations, such as during times of rapidly changing glucose levels, if symptoms do not match the device reading, or to confirm hypoglycemia or impending hypoglycemia.[1,4]

IAP members stated that CGM is not presently considered a comparator to Freestyle Libre FGMS as public coverage of this technology in Canada is currently limited. IAP members indicated that some private insurers may reimburse this technology for certain clinical situations. Compared to FGMS, the panel indicated that CGM offers the ability for patients to be informed by alarms of changes in glycemic level (e.g., hypoglycemia and hyperglycemia) and take necessary action. Both technologies allow for glycemic trend analysis with multiple data points.

Implementation Issue 3 (anticipated improved outcomes)

Implementation advice panellists noted that the HTAs found limited scientific evidence of glycemic benefits with the use of FGMS. These benefits consisted in the following two clinical end points:

- reduced frequency and duration of hypoglycemia in adults with T1D as well as in adults with T2D using IIT.
- improved time spent in target glycemic range in adults with T1D.

Acknowledging findings from the two HTAs, IAP members clarified that the main anticipated change in outcome of using Freestyle Libre FGMS is to improve hypoglycemia events, more specifically to reduce the frequency and duration of these events:

- some IAP members, however, indicated that recent evidence, mainly from observational studies, has suggested that the use of FGMS may also improve A1C and quality of life measures.

Other clinically relevant benefits of using FGMS, compared with using SMBG, are enhanced patient comfort, convenience, and independence as well as improved patient compliance in testing and better disease management due to availability of multiple, frequent data points for the analysis of glycemic trends. The latter statement is based on the observation that, for individuals on IIT, the quality of diabetes management is directly related to the frequency of glycemic testing and the use of related glycemic results to inform insulin dosing.

In addition, during the consultation, IAP members:

- stressed that, in all clinical situations, patients should be willing and able to learn how to use Freestyle Libre FGMS to improve diabetes management. It is therefore appropriate that access to this device be conditional on patients successfully completing a training session on the use of this technology and on self-management of insulin regimens. Such training would ideally be provided by a certified diabetes educator. If such services are not available close to the residence of a patient, alternative approaches could include teaching offered at local pharmacies, use of online training programs, or teaching provided by other qualified providers, including through industry-sponsored training programs.
- indicated that it would be reasonable for drug plans to implement a process to ensure the optimal use of FGMS; that is, carrying out a periodic review of patients to verify that the desired glycemic targets and frequency of scanning are achieved after using Freestyle Libre FGMS for a certain time period. Failure of patients to achieve the targeted scanning frequency and desired glycemic level could result in coverage discontinuation.

Other Discussion Points

With respect to the HTAs included in the Technology Review report, the IAP noted that scientific evidence on FGMS is still limited; provincial HTAs generally evaluated this evidence to be of very low to moderate quality (using the GRADE methodology). There was also a small number of studies available on FGMS. Acknowledging the limitations in the quantity and quality of the available scientific evidence, the panel indicated that the main advantage of FGMS, compared to SMBG (which involves use of test strips and blood from finger pricks to assess glycemic control), is the ability to analyze trends in glycemic control over time, which may have the potential to improve disease management

for patients on insulin therapy, specifically by reducing the frequency and duration of hypoglycemia events.

The panel identified several key clinical characteristics of patients with diabetes who could potentially derive greater benefit from FGMS compared with SMBG. These characteristics include:

- the need for IIT
- a requirement for frequent glycemic testing
- the presence of practical disease management challenges, such as difficulty performing multiple glycemic tests daily.

In addition, the panel indicated that patients with T1D may potentially derive a greater benefit from FGMS with respect to hypoglycemia but also emphasized that patients with T2D with the aforementioned characteristics would also be expected to derive benefit from using FGMS.

IAP members noted that the reimbursement of FGMS for patients with diabetes could potentially have a high budget impact for public drug plans. Based on data presented in the companion Technology Review report on FGMS, funding of this technology could be associated with additional estimated annual treatment costs to jurisdictional drug plans ranging from $627 to $1,241 per patient with T1D and T2D, respectively. IAP members suggested that individual jurisdictions could mitigate the potentially high expenditure for FGMS by reimbursing this technology only for those patients who are most likely to benefit because they are unable to effectively manage their disease using SMBG.

IAP members stressed it is important that patients use the FGMS device correctly in order to optimize the potential benefits of this technology. This could be achieved by providing support to patients to facilitate the development of technical knowledge of how to use Freestyle Libre FGMS, and by ensuring that patients use this device to improve the management of their condition. The panel suggested that public drug plans ensure that patients successfully complete a training program and that they develop a system to verify that patients achieve glycemic and testing frequency targets. Patients achieving these targets would be expected to improve their diabetes management.

A limitation of this work is that scientific evidence on the effect of FGMS on patient relevant outcomes is still relatively scarce, though growing. In addition, the HTAs used as the main source of information were completed in October 2018 (INESSS) and December 2019 (HQO), respectively. As such, potential new studies published within the last few months were not captured. On the other hand, as these two HTAs were conducted by Canadian jurisdictional organizations, IAP members could rely on their quality and relevance to inform policy decision in the Canadian context. Further, the HTAs considered both the clinical and economic perspectives.

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Appendix 1: Questionnaire Submitted to the Implementation Advice Panel

1.1 Please describe the population that would be expected to benefit most from using a FGMS to monitor their glycemia.

Focus on the Canadian context.
Please include a detailed description of key characteristics of these patients.

Response:
Click here to enter response.

1.2 Based on your response to question 1.1, please describe the existing method in clinical practice these patients are currently using to monitor their glycemia.

Focus on the Canadian context, accounting for not only clinical benefits but also ease of access for patients through public, private, and out-of-pocket payment.

Response:
Click here to enter response.

1.3 Compared to the most clinically relevant alternative identified in question 1.2, please describe the main benefits of using a FGMS for the population identified in question 1.1.

Please describe the place in therapy of the FGMS in the Canadian clinical practice setting. Also, please indicate whether the re are any treatment gaps associated with the use of the most clinically relevant alternative method to monitor glycemia identified in question 1.2. that this new technology may fill for this population.

Response:
Click here to enter response.