

Protocol

Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid

(10120)

Medical Benefit		Effective Date: 01/01/18	Next Review Date: 09/18
Preauthorization	Yes	Review Dates: 07/07, 07/08, 07/09, 01/10, 01/11, 01/12, 01/13, 05/13, 01/14, 05/14, 03/15, 03/16, 03/17, 09/17, 11/17	

Preauthorization is required for continuous, long-term monitoring.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> With type 1 diabetes who are willing and able to use the device, and have adequate medical supervision 	Interventions of interest are: <ul style="list-style-type: none"> Long-term (continuous) glucose monitoring 	Comparators of interest are: <ul style="list-style-type: none"> Self-monitoring of blood glucose 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Morbid events Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With type 1 diabetes and impaired hypoglycemia awareness and/or a history of recurrent unexplained severe hypoglycemia 	Interventions of interest are: <ul style="list-style-type: none"> Long-term (continuous) glucose monitoring 	Comparators of interest are: <ul style="list-style-type: none"> Self-monitoring of blood glucose 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Morbid events Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With type 1 diabetes 	Interventions of interest are: <ul style="list-style-type: none"> Short-term (intermittent) glucose monitoring 	Comparators of interest are: <ul style="list-style-type: none"> Self-monitoring of blood glucose 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Morbid events Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With type 2 diabetes 	Interventions of interest are: <ul style="list-style-type: none"> Long-term (continuous) glucose monitoring 	Comparators of interest are: <ul style="list-style-type: none"> Self-monitoring of blood glucose 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Morbid events Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> Who are pregnant with diabetic complications 	Interventions of interest are: <ul style="list-style-type: none"> Long-term (continuous) glucose monitoring 	Comparators of interest are: <ul style="list-style-type: none"> Self-monitoring of blood glucose 	Relevant outcomes include: <ul style="list-style-type: none"> Symptoms Morbid events Quality of life Treatment-related morbidity

Description

Tight glucose control in patients with diabetes has been associated with improved health outcomes. Several devices are available to measure glucose levels automatically and frequently (e.g., every five to 10 minutes). The devices measure glucose in the interstitial fluid and are approved as adjuncts to traditional self-monitoring of blood glucose levels. Devices can be used on an intermittent (short-term) basis or a continuous (long-term) basis.

Summary of Evidence

For individuals who have type 1 diabetes who are willing and able to use the device, and have adequate medical supervision, who receive long-term continuous glucose monitoring (CGM), the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, morbid events, quality of life, and treatment-related morbidity. Systematic reviews have generally found that, at least in the short-term, long-term CGM resulted in significantly improved glycemic control for adults and children with type 1 diabetes, particularly highly compliant patients. Recently published evidence has further demonstrated a clinically meaningful and significant benefit for use of long-term CGM in type 1 diabetics particularly for appropriately selected patients who are expected to adhere to use of the CGM. A 2017 individual patient data analysis, using data from 11 RCTs, found that reduction in hemoglobin A_{1c} (HbA_{1c}) levels was significantly greater with real-time CGM compared with a control intervention. Two newly added RCTs in patients who used multiple daily insulin injections and were highly compliant with CGM devices during run-in phases found that CGM was associated with a larger reduction in HbA_{1c} levels than previous studies. One of the two RCTs prespecified hypoglycemia-related outcomes and reported that time spent in hypoglycemia was significantly less in the CGM group. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have type 1 diabetes and impaired hypoglycemia awareness and/or a history of recurrent unexplained severe hypoglycemia who receive long-term CGM, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, morbid events, quality of life, and treatment related morbidity. Although meta-analyses of RCTs on CGM have generally not shown a significant difference in hypoglycemia outcomes between CGM and self-monitored blood glucose, those RCTs included a variety of patients and did not focus on patients at highest risk of hypoglycemia. A recently added 2016 crossover RCT that included only patients with impaired awareness of hypoglycemia found significantly improved hypoglycemia outcomes during the phase that a long-term CGM device was used compared with self-monitored blood glucose. Findings from this trial can be reasonably extrapolated to a related group of patients at increased risk of severe hypoglycemia (i.e., patients who have a history of recurrent, severe unexplained hypoglycemia) who would benefit from long-term CGM with alerts to provide earlier recognition of hypoglycemia to guide management that may improve health outcomes through avoided, reduced or less severe episodes of hypoglycemia. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have type 1 diabetes who receive short-term (intermittent) glucose monitoring, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, morbid events, quality of life, and treatment-related morbidity. The evidence for intermittent short-term monitoring on glycemic control is mixed, and there is no definite improvement in HbA_{1c} levels. Studies have not shown an advantage for intermittent glucose monitoring in reducing severe hypoglycemia events, but the number of events reported is generally small and effect estimates imprecise. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have type 2 diabetes who receive long-term CGM, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, morbid events, quality of life, and treatment related morbidity. Systematic reviews of three to four RCTs have found statistically significant benefits from CGM in terms of glycemic control. However, the degree of HbA_{1c} reduction and the difference in HbA_{1c} reduction between groups may not be clinically significant. In addition, the small number of RCTs and variability among interventions make it difficult to identify an optimal approach to CGM or subgroup of type 2 diabetes patients who might benefit. Moreover, studies of CGM in patients with type 2 diabetes have generally not addressed the clinically important issue of severe hypoglycemia. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are pregnant with diabetic complications who receive long-term CGM, the evidence includes several RCTs. Relevant outcomes are symptoms, morbid events, quality of life, and treatment related morbidity. Only a few RCTs have been published on CGM in pregnancies complicated by diabetes. Two of three RCTs that assessed large-for-gestational age infants as a primary or a secondary outcome did not find a significantly lower rate of larger infants delivered by women who used CGM. Other outcomes (e.g., maternal glycemic control, neonatal hypoglycemia) tended not to be significantly improved with CGM. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy

Continuous (i.e., long-term) monitoring of glucose levels in interstitial fluid, including real-time monitoring, as a technique of diabetic monitoring, may be considered **medically necessary** when the following situations occur, despite use of best practices:

- patients with type 1 diabetes who have demonstrated an understanding of the technology, are motivated to use the device correctly and consistently, are expected to adhere to a comprehensive diabetes treatment plan supervised by a qualified provider, and are capable of using the device to recognize alerts and alarms; or
- patients with type I diabetes mellitus who have recurrent, unexplained, severe, (generally blood glucose levels less than 50 mg/dl) hypoglycemia or impaired awareness of hypoglycemia that puts the patient or others at risk; or
- patients with poorly controlled type I diabetes mellitus who are pregnant. Poorly controlled type I diabetes mellitus includes unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis.

Other uses of continuous monitoring of glucose levels in interstitial fluid as a technique of diabetic monitoring are considered **investigational**.

Intermittent monitoring (i.e., 72 hours) of glucose levels in interstitial fluid may be considered **medically necessary** in patients with type I diabetes mellitus whose diabetes is poorly controlled, despite current use of best practices (see Policy Guidelines). Poorly controlled type I diabetes mellitus includes the following clinical situations: unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis.

Intermittent monitoring of glucose levels in interstitial fluid may also be considered **medically necessary** in patients with type I diabetes mellitus prior to insulin pump initiation to determine basal insulin levels.

Policy Guidelines

Several insulin pump systems (e.g., Paradigm® REAL-Time System) have a built-in CGM. This protocol only evaluates the CGM; it does not evaluate insulin pumps. Insulin pump systems with a built-in CGM and a low glucose suspend (LGS) feature, are addressed in the Artificial Pancreas Device Systems Protocol.

Best practices in diabetes control for patients with diabetes mellitus include compliance with a regimen of four or more fingersticks each day and use of an insulin pump. During pregnancy, three or more insulin injections daily could also be considered best practice for patients not on an insulin pump prior to the pregnancy. Prior use of an intermittent (72-hour) glucose monitor would be considered a part of best practices for those considering use of a continuous glucose monitor.

Women with type I diabetes mellitus taking insulin who are pregnant or about to become pregnant with poorly controlled diabetes are another subset of patients to whom the policy statement on intermittent monitoring may apply.

Intermittent monitoring is generally conducted in 72-hour periods. It may be repeated subsequently depending on the patient's level of diabetes control.

The strongest evidence exists for use of CGM devices in patients age 25 and older. However, age may be a proxy for motivation and good control of disease, so it is also reasonable to select patients based on their ability to self-manage their disease, rather than age.

Providers board certified in endocrinology and/or providers with a focus on the practice of diabetes care may be considered qualified to evaluate and oversee individuals for continuous (i.e., long-term) monitoring.

Medicare Advantage

Therapeutic CGMs (continuous glucose monitor) and related supplies are considered **medically necessary** when all of the following coverage criteria (1-6) are met:

1. The patient has diabetes mellitus; and,
2. The patient has been using a BGM (blood glucose monitor) and performing frequent (four or more times a day) testing; and,
3. The patient is insulin-treated with multiple (three or more) daily injections of insulin or a covered continuous subcutaneous insulin infusion (CSII) pump; and,
4. The patient's insulin treatment regimen requires frequent adjustment by the patient on the basis of BGM or CGM testing results; and,
5. Within six (6) months prior to ordering the CGM, the treating practitioner has an in-person visit with the patient to evaluate their diabetes control and determined that criteria (1-4) above are met; and,
6. Every six (6) months following the initial prescription of the CGM, the treating practitioner has an in-person visit with the patient to assess adherence to their CGM regimen and diabetes treatment plan.

If any of coverage criteria (1-6) are not met, the CGM will be denied as **not medically necessary**.

Background

The advent of blood glucose monitors for use by patients in the home revolutionized the management of diabetes. Using fingersticks, patients can monitor their blood glucose levels both to determine the adequacy of

hyperglycemia control and to evaluate hypoglycemic episodes. Tight diabetic control, defined as a strategy involving frequent glucose checks and a target hemoglobin A_{1c} (HbA_{1c}) level in the range of 7%, is now considered standard of care for diabetic patients. RCTs assessing tight control have demonstrated benefits for patients with type 1 diabetes in decreasing microvascular complications. The impact of tight control on type 1 diabetes and on macrovascular complications such as stroke or myocardial infarction is less certain.

Tight glucose control requires multiple daily measurements of blood glucose (i.e., before meals and at bedtime), a commitment that some patients may be unwilling or unable to meet. In addition, the goal of tight glucose control has to be balanced with an associated risk of hypoglycemia. Hypoglycemia is known to be a risk in patients with type 1 diabetes. While patients with insulin-treated type 2 diabetes may also experience severe hypoglycemic episodes, there is a lower relative likelihood of severe hypoglycemia compared to patients with type 1 diabetes.^{1,2} An additional limitation of periodic self-measurements of blood glucose is that glucose levels are seen in isolation, and trends in glucose levels are undetected. For example, while a diabetic patient's fasting blood glucose level might be within normal values, hyperglycemia might be undetected postprandially, leading to elevated hemoglobin A_{1c} values.

Recently, measurements of glucose in interstitial fluid have been developed as a technique to measure glucose values throughout the day, producing data that show the trends in glucose levels. Although devices measure glucose in interstitial fluid on a periodic rather than a continuous basis, this type of monitoring is referred to as continuous glucose monitoring.

Several devices have received approval from the U.S. Food and Drug Administration (FDA). The first two approved devices were the Continuous Glucose Monitoring System (MiniMed), which uses an implanted temporary sensor in the subcutaneous tissues, and the GlucoWatch G2[®] Biographer, an external device worn like a wristwatch that measures glucose in interstitial fluid extracted through the skin by electric current (referred to as reverse iontophoresis).

Devices subsequently approved include those for pediatric use and those with, e.g., more advanced software, more frequent measurements of glucose levels, or more sophisticated alarm systems. Devices initially measured interstitial glucose every five to 10 minutes and stored data for download and retrospective evaluation by a clinician. With currently available devices, the time intervals at which interstitial glucose is measured ranges from every one to two minutes to five minutes and most provide measurements in real-time directly to patients. While CGM potentially eliminates or decreases the number of required daily fingersticks, it should be noted that, according to the FDA labeling, monitors are not intended as an alternative to traditional self-monitoring of blood glucose levels but rather as adjuncts to monitoring, supplying additional information on glucose trends that are not available from self-monitoring. In addition, devices may be used intermittently (i.e., for periods of 72 hours), or continuously (i.e., on a long-term basis).

In addition to stand-alone continuous glucose monitors, several insulin pump systems have included a built-in CGM. This protocol addresses CGM devices, not the insulin pump portion of these systems.

Regulatory Status

Several CGM systems have been approved by the FDA through the premarket approval process (see Table 1).

Table 1. CGM Systems Approved by the Food and Drug Administration

Device	Manufacturer	Approval	Indications
Continuous Glucose Monitoring System (CGMS [®])	MiniMed	1999	3-d use in physician's office
GlucoWatch G2 [®] Biographer ^a		2001	
Guardian [®] -RT (Real-Time) CGMS	MiniMed	2005	

Device	Manufacturer	Approval	Indications
	(now Medtronic)		
Dexcom® STS CGMS system	Dexcom	2006	
Paradigm® REAL-Time System (second generation called Paradigm Revel System)	MiniMed (now Medtronic)	2006	System integrates a CGM with a Paradigm insulin pump
FreeStyle Navigator® CGM System	Abbott	2008	
Dexcom® G4 Platinum	Dexcom	2012 2014	Adults ≥ 18 y; can be worn for up to seven days; Expanded use to include patients with diabetes two-17 years
Dexcom® G5 Mobile CGM		2016 ^b	Replacement for fingerstick blood glucose testing in patients ≥ two years. System requires at least two daily fingerstick tests for calibration purposes, but additional fingersticks are not necessary because treatment decisions can be made based on device readings. ³

CGM: continuous glucose monitoring.

^a Neither the GlucoWatch nor the autosensors have been available since July 2008.

^b As a supplement to the G4 premarketing approval.

FDA product code: MDS, PQF.

Related Protocol

Artificial Pancreas Device Systems

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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