Medicare Policy

Title: Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid

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Tight glucose control in patients with diabetes has been associated with improved outcomes. Several devices are available to measure glucose levels automatically and frequently (e.g., every 5-10 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.

**BACKGROUND**

The advent of blood glucose monitors for use by patients in the home over 20 years ago revolutionized the management of diabetes. Using fingersticks, patients could monitor their blood glucose level 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 HgA\(_{1c}\) in the range of 7%, is now considered standard of care for diabetic patients. Randomized controlled trials (RCTs) of tight control have demonstrated benefits for type I diabetics in decreasing microvascular complications. The impact of tight control on type II diabetics and on macrovascular complications such as stroke or myocardial infarction (MI) is less certain.

However, tight glucose control requires multiple measurements of blood glucose each day (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. An additional limitation of periodic self-measurements of blood glucose is that glucose values 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 of automatically measuring glucose values throughout the day, producing data that show the trends in glucose measurements, in contrast to the isolated glucose
measurements of the traditional blood glucose measurements. 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 (CGM).

Several devices have received U.S. Food and Drug Administration (FDA) approval. The first two approved devices were the Continuous Glucose Monitoring System (CGMS®) (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 with an electric current (referred to as reverse iontophoresis).

Additional devices that have subsequently been approved include those for pediatric use and those with more advanced software, more frequent measurements of glucose levels, more sophisticated alarm systems, etc. Devices initially measured interstitial glucose every 5 to 10 minutes and, with currently available devices the time intervals at which interstitial glucose is measured ranges from every 1-2 minutes to 5 minutes. While continuous glucose monitors potentially eliminate or decrease the number of required daily fingersticks, it should be noted that, according to the FDA labeling, monitors are not intended to be an alternative to traditional self-monitoring of blood glucose levels but rather provide adjunct, supplying additional information on glucose trends that are not available from self-monitoring. In addition, it is important to note that devices may be used intermittently, eg, time periods of 72 hours, or on a long-term basis.

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

**REGULATORY STATUS**

Several continuous glucose monitoring systems have been approved by the FDA through the premarket approval process:

- The Continuous Glucose Monitoring System (CGMS®) (MiniMed) in 1999 (approved for 3-day use in a physician’s office).
- The GlucoWatch G2® Biographer in 2001. Of note, neither the GlucoWatch nor the autosensors have been available after July 31, 2008.
- The Guardian®-RT (Real-Time) CGMS (Medtronic, MiniMed) in July 2005. (MiniMed was purchased by Medtronic).
- The DexCom® STS CGMS system (DexCom) was approved by the FDA in March 2006.
- The Paradigm® REAL-Time System (Medtronic, MiniMed) was approved by the FDA in 2006. This system integrates a continuous glucose monitor with a Paradigm insulin pump. The second generation integrated system is called the MiniMed Paradigm Revel System.
- The FreeStyle Navigator® CGM System (Abbott) was approved in March 2008.
• The DexCom G4 Platinum (DexCom) CGM was approved for use in adults 18 years and older in October 2012. The device can be worn for up to 7 days. In February 2014, FDA expanded use of the Dexcom Platinum CGM to include patients with diabetes, age 2 to 17 years old.
POLICY

A. Intermittent monitoring, ie, up to 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:

1. Unexplained hypoglycemic episodes;
2. Hypoglycemic unawareness;
3. Suspected postprandial hyperglycemia; and
4. Recurrent diabetic ketoacidosis.

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

C. Continuous, ie, 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:

1. Patients with type I diabetes who have recurrent, unexplained, severe (generally blood glucose levels less than 50 mg/dL) hypoglycemia for whom hypoglycemia puts the patient or others at risk, or
2. Patients with type I diabetes who have recurrent diabetic ketoacidosis (DKA) requiring emergency room visits and admissions.
3. Patients with type I diabetes who are pregnant whose diabetes is poorly controlled. Poorly controlled type I diabetes includes unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis.

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

**Note:** Hypoglycemia unawareness is reversible. Meticulous avoidance of hypoglycemic for several weeks is sufficient to restore awareness of hypoglycemia. Hypoglycemia Anticipation, Awareness and Treatment Training/Blood Glucose Awareness Training (HAATT/BGAT) has been proven to reduce the occurrence of severe hypoglycemia.


*Contains Public Information*
Policy Guidelines

1. Several insulin pump systems (e.g., Paradigm® REAL-Time System) have a built-in continuous glucose monitor (CGM). This policy is evaluating the CGM-device only; the policy does not evaluate insulin pumps. In the case of insulin pumps systems with a built-in CGM and low glucose suspend (LGS) feature, the CGM device and the low glucose suspend feature are evaluated in the policy, not the insulin pump.

2. Best practices in diabetes control for patients with diabetes mellitus include compliance with a regimen of 4 or more fingersticks each day and use of an insulin pump or multiple daily injections. Compliance will also be required for other aspects of diabetic management including insulin bolusing and diet. During pregnancy, 3 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.

3. Individuals with type I diabetes mellitus 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.

4. Intermittent monitoring is generally conducted in 72-hour periods. It may be repeated at a subsequent time depending on the patient’s level of diabetes control.

5. 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.

RATIONALE

A TEC Assessment was published in 2003. The most recent literature review was performed for the period through April 11, 2016. Following is a summary of the key literature to date.

Most of the discussion will focus on the clinical utility of continuous glucose monitoring (CGM) systems. That is, their ability to provide either additional information on glucose levels, leading to improved glucose control, or to improve the morbidity and mortality associated with clinically significant severe and acute hypoglycemic or hyperglycemic events. Because diabetic control encompasses numerous variables, including the diabetic regimen and patient self-management, randomized controlled trials (RCTs) are important to isolate the contribution of interstitial glucose measurements to overall diabetes management. Data on patients with types 1 and 2 diabetes are discussed separately.

Type 1 Diabetes

This evidence review includes RCTs that report on outcomes of CGM devices. We categorized CGM devices as continuous, long-term, monitoring devices by the patient to direct insulin
regimens, and intermittent (ie, 72 hour), short-term monitoring used by the provider to optimize management.

**CGM Devices for Long-Term Use**
A number of meta-analyses of RCTs on CGM for long-term, daily use in treating type 1 diabetes have been published. These meta-analyses focused on slightly different populations, and some did not separate long-term CGM from intermittent glucose monitoring. The most recent meta-analysis, published by Yeoh et al (2015), addressed a broad range of interventions to restore hypoglycemia awareness in adults with type 1 diabetes (ie, educational, technological, and pharmacologic interventions) and did not identify any RCTs focusing on CGM for hypoglycemia unawareness.

At least 2 meta-analyses have reported separate subgroup analyses for long-term CGM. A 2012 Cochrane review of CGM in type I diabetes in adults and children included RCTs comparing CGM with conventional self-monitored blood glucose (SMBG). In pooled analysis (6 studies; 963 patients) of studies of long-term CGM, the average decline in HbA1c levels 6 months after baseline was statistically significantly larger for CGM users than SMBG users (mean difference [MD] change, -0.2%; 95% confidence interval [CI], -0.4% to -0.1%), but there was no difference in decline in HbA1c levels at 12 months (1 study, 154 patients; MD change, 0.1; 95% CI, -0.5 to 0.7). In meta-analysis of 4 RCTs (689 patients), there was no significant difference in risk of severe hypoglycemia between CGM and SMBG users and the confidence interval for the relative risk (RR) was wide (RR=1.05; 95% CI, 0.63 to 1.77) indicating lack of precision in estimating the effect of CGM on hypoglycemia risk. The reviewers were unable to compare longer term change in HbA1c levels or hypoglycemia outcomes for real-time CGM. Trials reporting results by compliance subgroups found larger treatment effects in highly compliant patients.

A 2011 meta-analysis of RCTs on CGM included trials conducted in adults and children with type 1 diabetes. Reviewers selected studies having a minimum of 12 weeks of follow-up and requiring patients be on intensive insulin regimens. Studies compared CGM to SMBG; there was no restriction on type of CGM device, but CGM readings had to be used to adjust insulin dose or modify diet. Fourteen RCTs met eligibility criteria. Study durations ranged from 3 to 6 months. Baseline mean HbA1c levels ranged from 6.4% to 10%. Five included studies found a statistically significant decrease in HbA1c levels favoring CGM while 9 did not. In a pooled analysis, there was a statistically significant reduction in HbA1c levels with CGM compared with SMBG (weighted mean difference [WMD] = -0.26%; 95% CI, -0.34% to -0.19%). For the subgroup of 7 studies that reported on long-term CGM, this difference was statistically significant (WMD = -0.26; 95% CI, -0.34 to -0.18). In a subgroup analysis by age, there were significant reductions in HbA1c levels with CGM in studies of adults (n=5; WMD = -0.33; 95% CI, -0.46 to -0.20) and in studies with children and/or adolescents (n=8; WMD = -0.25; 95% CI, -0.43 to -0.08). Four of the studies provided data on the frequency of hypoglycemic episodes. Pooled results showed a significant reduction in hypoglycemic events for CGM versus SMBG (standardized mean difference, -0.32; 95% CI, -0.52 to -0.13). Five of the studies reported the percentage of patients with severe hypoglycemic episodes and there were no differences in the percentage of patients with severe hypoglycemic episodes using CGM and SMBG in any of them.

Of the RCTs included in these meta-analyses, the largest were 2 sponsored by the Juvenile Diabetes Research Foundation (JDRF). In 2008, JDRF published results of a study that randomly assigned 322 adults and children with type 1 diabetes to CGM or self-(home) monitoring.
With HbA$_1c$ as the primary outcome measure, there was a significant difference among patients 25 years of age or older that favored CGM (MD HbA$_1c$, 0.53%), while the difference between groups was not statistically significant for those ages 15 to 24 years or 8 to 14 years. The population in this study had relatively well-controlled diabetes in that entry criterion was glycated hemoglobin of 7% to 10%, but approximately 70% had levels between 7% and 8%; in addition, more than 70% of patients were using an insulin pump. No significant differences were noted in rates of hypoglycemic events, but the study was likely not sufficiently large to detect potential differences. The authors also reported that monitor use was greatest in those patients ages 25 or older (83% of patients used the monitor ≥6 d/wk).

The investigators also conducted a nonblinded, single-arm, 6-month extension to the randomized trial in which patients in the control group were offered a CGM device. A total of 214 (98%) of 219 in the control group participated in the extension. This included 80 (37%) who were at least 25 years old, 73 (34%) who were 15- to 24-year old, and 61 (29%) who were 8- to 14-year old. The mean HbA$_1c$ level at the time of initiation of CGM use was 7.4%. Patients were instructed to use the device on a daily basis. Among the 154 patients with baseline HbA$_1c$ levels at least 7%, there was a significant decrease in HbA$_1c$ levels 6 months after initiating device use in the older age group (mean change in HbA$_1c$ -0.4%±0.5%; p<0.001). HbA$_1c$ levels did not decrease significantly in the 15- to 24-year-olds (0.01%±0.7%, p=0.95) or in the 8- to 14-year-olds (0.02%±0.7%, p=0.85). Greater decrease in HbA$_1c$ levels was associated with more frequent use of the CGM device (p=0.001, adjusted for age group). Frequency of device use tended to decrease over time, with less decrease in the older age group. At month 6, median use of CGM devices was 6.5 days per week among the older age group, 3.3 days among the 15- to 24-year-olds, and 3.7 days per week among the children. During the 6-month extension, the rate of severe hypoglycemic events was 15 per 100 person-years of follow-up.

An additional randomized trial by JDRD, published in 2009, studied the potential benefits of CGM in the management of adults and children with well-controlled type 1 diabetes. In this trial, 129 adults and children with intensively treated type 1 diabetes (age range, 8-69 years) and HbA$_1c$ levels less than 7.0% were randomly assigned to continuous or standard glucose monitoring (control) for 26 weeks. The main trial outcomes were time with glucose level at or below 70 mg/dL, HbA$_1c$ level, and severe hypoglycemic events. At 26 weeks, median time with biochemical hypoglycemia (≤70 mg/dL) did not differ significantly between the CGM (54 min/d) and the control group (91 min/d; p=0.16). Time out of range (≤70 mg/dL or >180 mg/dL) was significantly lower in the CGM group (377 min/d) than in the control group (491 min/d; p=0.003). There was a significant treatment group difference favoring the CGM group in mean HbA$_1c$ level at 26 weeks adjusted for baseline values. One or more severe hypoglycemic events occurred in 10% and 11% of the 2 groups, respectively (p=NS). This small study had mixed findings (statistically significant benefit of CGM on time out of range and mean HbA$_1c$ level at follow-up, but not on biochemical hypoglycemia or severe hypoglycemic events).

Since publication of the 2012 Cochrane review, 4 RCTs were identified that addressed long-term CGM.

In 2012, Battelino et al reported on a randomized crossover study to evaluate the efficacy of adding CGM to insulin pump therapy in adults and children with type 1 diabetes. Eligible patients ranged in age from age 6 to 70 years and their HbA$_1c$ levels ranged from 7.5% to 9.5%. A total of 153 subjects were randomized to 6 months of “off” followed by 6 months of “on” monitoring
(n=76) or to an on/off sequence (n=77). For the trial’s primary outcome, after 6 months of treatment, the mean HbA$_{1c}$ level was 8.04% in the “on” arm and 8.47% in the “off” arm (MD = -0.43%; 95% CI, -0.32% to -0.55%; p<0.001). Rates of severe hypoglycemic events did not differ between arms (5.70 per 100 patient-years in the “on” arm vs 2.83 per 100 patient-years in the “off” arm, p=0.40).

Also in 2012, Mauras et al reported on an RCT that evaluated real-time CGM in the management of young children (age range, 4-10 years) with type 1 diabetes. A total of 146 children (mean age, 7.5 years) were randomized to CGM or usual care. At baseline, 30 (42%) children had an HbA$_{1c}$ level of at least 8%. The primary outcome was clinical success, defined as reduction in HbA$_{1c}$ levels by at least 0.5% without occurrence of severe hypoglycemia at 26 weeks. Clinical success was attained by 19% in the CGM group and 28% in the usual care group (p=0.17). Mean change in HbA$_{1c}$ levels, a secondary outcome, did not differ significantly between groups (-0.1 in each group, p=0.79).

A 2014 RCT by Little et al comparing real-time monitoring with SMBG in a sample of 96 patients with type 1 diabetes, using a 2×2 factorial design, reported no significant differences in patient satisfaction or perceptions of hypoglycemia between the groups. However, the trial did not report on HbA$_{1c}$ levels or other metrics of diabetes control. An additional pilot study by Sequiera et al (2013) with a randomized crossover design that evaluated CGM in 25 patients did not report improvements in HbA$_{1c}$ levels with real-time monitoring, but this study was likely underpowered to detect a difference.

Glucose Monitoring Devices for Intermittent, Short-Term Use
The meta-analyses of glucose monitoring devices for type 1 diabetes have tended to combine studies of intermittent glucose monitoring with studies of long-term CGM. For this body of evidence, there is variability in the definitions of intermittent monitoring and the specific monitoring protocols used. In addition, many of the trials of intermittent monitoring included additional interventions to optimize glucose control such as education and lifestyle modifications.

Two meta-analyses were identified that reported separate subgroup analyses for intermittent monitoring. In the 2012 Cochrane review, 4 studies (total N=216 patients) compared real-time intermittent glucose monitoring systems to SMBG, and the pooled effect estimate for change in HbA$_{1c}$ levels at 3 months was not statistically significant (MD change, -0.18; 95% CI, -0.42 to 0.05). The 2011 meta-analysis of RCTs on CGM described previously also included a separate analysis of 8 RCTs of intermittent monitoring. On pooled analysis, there was a statistically significant reduction in HbA$_{1c}$ levels with intermittent glucose monitoring compared with SMBG (WMD = -0.26; 95% CI, -0.45 to -0.06).

The largest RCT was the 2009 Management of Insulin-Treated Diabetes Mellitus (MITRE) trial, published by Newman et al, which evaluated whether the additional information provided by minimally invasive glucose monitors resulted in improved glucose control in patients with poorly controlled insulin-requiring diabetes. This was a 4-arm RCT conducted at secondary care diabetes clinics in 4 hospitals in England. In this trial, 404 people over the age of 18 years, with insulin-treated diabetes (types 1 or 2) for at least 6 months, who were receiving 2 or more injections of insulin daily, were eligible. Most (57%) participants had type 1 diabetes (41% had type 2 diabetes, 2% were classified as “other”). Participants had to have 2 HbA$_{1c}$ values of at least 7.5% in the 15 months before trial entry and were randomized to 1 of 4 groups. Two
groups received minimally invasive glucose monitoring devices (GlucoWatch Biographer or MiniMed Continuous Glucose Monitoring System [CGMS]). Intermittent glucose monitoring was used (ie, monitoring was performed over several days at various points in the study). These groups were compared with an attention control group (standard treatment with nurse feedback sessions at the same frequency as those in the device groups) and a standard control group (reflecting common practice in the clinical management of diabetes). Change in HbA1c levels from baseline to 3, 6, 12, and 18 months was the primary indicator of short- to long-term efficacy. At 18 months, all groups demonstrated a decline in HbA1c levels from baseline. Mean percentage changes in HbA1c levels were -1.4 for the GlucoWatch group, -4.2 for the CGMS group, -5.1 for the attention control group, and -4.9 for the standard care control group. In the intention-to-treat analysis, no significant differences were found between any groups at any assessment times. There was no evidence that the additional information provided by the devices resulted in any change in the number or nature of treatment recommendations offered by the nurses. Use and acceptability indicated a decline for both devices, which was most marked in the GlucoWatch group by 18 months (20% still using GlucoWatch vs 57% still using the CGMS). In this study of unselected patients, glucose monitoring (CGMS on an intermittent basis) did not lead to improved clinical outcomes.

Section Summary: Type 1 Diabetes
Numerous RCTs and several systematic reviews of RCTs have evaluated CGM in patients with type 1 diabetes. For long-term CGM, the RCTs have reported mixed results, but most have reported improvement in glucose control, as measured by HbA1c levels for patients who used a CGM compared to standard monitoring. A 2012 Cochrane review reported that the improvement in HbA1c levels is in the range of 0.2% to 0.3%, and individual RCTs published since 2012 have corroborated that range of improvement. The clinical significance of this difference in HbA1c levels is uncertain. None of the RCTs or systematic reviews reported improvements in severe hypoglycemic episodes, but the number of events reported is generally small and effect estimates are imprecise. Due to the uncertainty whether the magnitude of effect is clinically significant, it is not possible to conclude whether outcomes are improved.

For intermittent, short-term monitoring there a few RCTs and systematic reviews. Some trials have reported improvements in glucose control for the intermittent monitoring group, but there are limitations to this body of evidence that preclude conclusions. The definitions of intermittent control and the specific monitoring protocols varied. In some studies, intermittent monitoring was part of a larger strategy aimed at optimizing glucose control, and the impact of monitoring cannot be separated from the impact of other interventions. Due to the limitations in this evidence base, it is not possible to conclude whether outcomes are improved.

Type 2 Diabetes
Two of the systematic reviews previously described also reported on the efficacy of CGM in patients with type 2 diabetes. Gandhi et al identified 3 RCTs studying patients with type 2 diabetes (1 study included both types of diabetes).5 There was a mix of patients with type 2 diabetes who did and did not require insulin. Two of the 3 trials evaluated retrospective CGM of different lengths and durations and the third evaluated real-time intermittent CGM. Patients in the studies had baseline HbA1c levels greater than 8%. In a meta-analysis of the 3 trials, there was a statistically significant reduction in HbA1c levels with CGM compared with SMBG in adults with type 2 diabetes (WMD = -0.70; 95% CI, -1.14 to -0.27). In 2013, Poolsup et al conducted a meta-analysis of 4 trials evaluating adults with type 2 diabetes.7 Three trials in Poolsup
overlapped with those of Gandhi; the remaining trial also evaluated real-time CGM but with a longer period of use (2 weeks on and 1 week off for 3 months). In a pooled analysis, CGM had greater efficacy in terms of HbA$_1c$ levels than SMBG. The pooled mean difference in HbA$_1c$ level was -0.31% (95% CI, -0.6% to 0.02%; p=0.04). Because of a lack of statistical heterogeneity among studies, subgroup analyses (eg, by type of CGM device) were not performed.

The Ehhardt et al (2011) study has the largest sample size (N=100) in the Poolsup systematic review (accounting for 45% of the weight in the pooled analysis of HbA$_1c$ levels). The trial evaluated intermittent use of a CGM device in adult patients with type 2 diabetes treated with diet/exercise and/or glycaemia-lowering medications but not prandial insulin who had an initial HbA$_1c$ level of at least 7% but not more than 12%. The study compared real-time continuous monitoring with the Dexcom device used for four 2-week cycles (2 weeks on/1 week off) with SMBG. The primary efficacy outcome was mean change in HbA$_1c$ levels. Mean (SD) HbA$_1c$ levels in the CGM group were 8.4% (1.5%) at baseline, 7.4% (1.0%) at 12 weeks, 7.3% (1.1%) at 24 weeks, and 7.7% (1.1%) at 52 weeks. In the SMBG group, these values (SD) were 8.2% (1.1%) at baseline, 7.7% (1.2%) at 12 weeks, 7.6% (1.3%) at 24 weeks, and 7.9% (1.4%) at 52 weeks. Over the course of the study, the reduction in HbA$_1c$ levels was significantly greater than in the SMBG group (p=0.04). After adjusting for potential confounders (eg, age, sex, baseline therapy, whether the individual started taking insulin during the study), the difference between groups over time remained statistically significant (p<0.001). The investigators also evaluated SMBG results from both groups. The mean proportion of SMBG tests less than 70 mg/dL were 3.6% in the CGM group and 2.5% in the SMBG group (p=0.06).

A 2016 RCT, published by Sato et al, included 34 patients with type 2 diabetes who were at least 20 years old and on insulin injection therapy, had HbA$_1c$ levels between 6.9% and 11.0% during the previous 3 months, with HbA$_1c$ fluctuations within 0.5%. All patients conducted SMBG and used a retrospective CGM device for 4 to 5 days before each of 3 clinic visits, 2 months apart. At clinic visits, patients were evaluated and suggestions made to improve glucose control by lifestyle changes and by changing medication doses. In the intervention group, but not the control group, patients and physicians had access to CGM data at the clinic visits. The primary end point was change in HbA$_1c$ levels, which did not differ significantly between groups at the end of the trial, compared with baseline, between the first and second visits or between the second and third visits. HbA$_1c$ levels changed little in either group. In the intervention group, the mean (SD) baseline HbA$_1c$ level was 8.2% (1.2%) and the mean final HbA$_1c$ level was also 8.2% (1.3%). Comparable percentages in the control group were 8.2% (0.9%) and 7.9% (0.8%). In this trial, conducted in Japan, decisions around medication doses were made only by the physician at clinic visits and practices may differ in other countries.

Section Summary: Type 2 Diabetes
There are fewer RCTs on CGM in patients with type 2 diabetes than for patients with type 1. Systematic reviews of 3 to 4 trials found statistically significant benefits of 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 makes it difficult to identify an optimal approach to CGM use or subgroup of type 2 diabetes patients who might benefit. Moreover, studies of CGM in patients with type 2 diabetes generally do not address the clinically important issue of severe hypoglycemia.
Pregnant Women With Diabetic Complications

In 2013, Voormolen et al published a systematic review of the literature on CGM during pregnancy. They identified 11 relevant studies. Two were RCTs. The 11 studies included a total of 534 women; the largest was an RCT (N=154). Seven used retrospective CGM; the remaining 4 studies used real-time CGM. The authors did not pool study findings; they concluded that the evidence is limited on the efficacy of CGM during pregnancy. The 2 published RCTs are described next.

The larger RCT was published by in 2013 by Secher et al in Denmark. The investigators randomized 154 women with type 1 (n=123) and type 2 (n=31) diabetes to real-time CGM in addition to routine pregnancy care (n=79) or routine pregnancy care alone (n=75). Patients in the CGM group were instructed to use the CGM device for 6 days before each of 5 study visits and were encouraged to use the devices continuously. Participants in both groups were instructed to perform 8 daily self-monitored plasma glucose measurements for 6 days before each visit. Baseline mean HbA1c levels were 6.6% in the CGM group and 6.8% in the routine care group. The 154 pregnancies resulted in 149 live births and 5 miscarriages. The prevalence of large-for-gestational age infants (at least 90th percentile), the primary study outcome, was 45% in the CGM group and 34% in the routine care group. The difference between groups was not statistically significant (p=0.19). In addition, no statistically significant differences were found between groups for secondary outcomes, including the prevalence of preterm delivery and the prevalence of severe neonatal hypoglycemia. Women in this trial had low baseline HbA1c levels, which might explain the lack of impact of CGM on outcomes. Other factors potentially contributing to the negative findings include the intensive SMBG routine in both groups and the relatively low compliance rate (64%) in the CGM group with the instruction of use the CGM devices for 6 days before each of 5 study visits.

In 2008, Murphy et al in the U.K. randomized 71 pregnant women with type 1 (n=46) and type 2 (n=25) diabetes to CGM or usual care. The intervention consisted of up to 7 days of CGM at intervals of 4 to 6 weeks between 8 weeks and 32 weeks of gestation. In addition to CGM, the women were advised to measure blood glucose levels at least 7 times a day. Baseline HbA1c (SD) levels were 7.2% (0.9%) in the CGM group and 7.4% (1.5%) in the usual care group. The primary study outcome was maternal glycemic control during the second and third trimesters. Mean HbA1c (SD) levels were consistently lower in the intervention arm, but differences between groups were not statistically significant at any time point. For example, between 28 weeks and 32 weeks of gestation, mean HbA1c levels were 6.1% (0.60%) in the CGM group and 6.4% (0.8%) in the usual care group (p=0.10). The prevalence of large-for-gestational age infants (at least 90th percentile) was a secondary outcome. Thirteen (35%) of 37 infants in the CGM group were large-for-gestational age compared with 18 (60%) of 30 in the usual care group. The odds ratio for reduced risk of a large-for-gestational age infant with CGM was 0.36 (95% CI, 0.13 to 0.98; p=0.05).

In addition to the systematic review, in 2016, Wei et al published an RCT on CGM in 120 women with gestational diabetes at 24 to 28 weeks. Patients were allocated to prenatal care plus CGM (n=58) or SMBG (n=62). The investigators assessed a number of end points and did not specify primary outcomes; a significance level of p less than 0.05 was used for all outcomes. The groups did not differ significantly in change in most outcomes including change in maternal HbA1c levels, rates of preterm delivery before the 35th gestational week, cesarean delivery rates, proportions...
of large-for-gestational age infants, or rates of neonatal hypoglycemia. Women in the CGM group gained significantly less weight than those in the SMBG group.

Section Summary: Pregnant Women With Diabetic Complications
Only a few RCTs have been published on GGM in pregnancies complicated by diabetes. Two of 3 RCTs that assessed large-for-gestational age infants as a primary or a secondary outcome did not find a significantly lower rates in women who used CGM. Other outcomes, such as maternal glycemic control and neonatal hypoglycemia tended not to be significantly improved with CGM.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 1.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01614262</td>
<td>Examining the Role of Continuous Glucose Monitoring (CGM) in Non-Insulin Treated Type 2 Diabetes</td>
<td>90</td>
<td>Dec 2015 (ongoing)</td>
</tr>
<tr>
<td>NCT01787903</td>
<td>The Effects of Real-time Continuous Glucose Monitoring on Glycemia and Quality of Life in Patients With Type 1 Diabetes Mellitus and Impaired Hypoglycemia Awareness</td>
<td>52</td>
<td>Apr 2016 (ongoing)</td>
</tr>
<tr>
<td>NCT02671968</td>
<td>Real-Time Continuous Glucose Monitoring (RT-CGM) in Patients With Type 1 Diabetes at High Risk for Low Glucose Values Using Multiple Daily Injections (MDI) in Germany (HYPODE-STUDY)</td>
<td>160</td>
<td>Dec 2017</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
* Denotes industry-sponsored or cosponsored trial.

SUMMARY OF EVIDENCE
For individuals who have type 1 diabetes who receive short-term (intermittent) glucose monitoring or 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 generally found that, at least in the short-term, long-term CGM resulted in improved glycemic control for adults and for children with type 1 diabetes, particularly highly compliant patients. The magnitude of improvement is small, in the range of 0.2% to 0.3%, and of uncertain clinical significance. There is little data on how effective CGM beyond 6 months. The evidence for intermittent short-term monitoring on glycemic control is mixed, and there is not a definite improvement in hemoglobin A1c (HbA1c) levels. Studies have not shown an advantage for glucose monitoring in reducing severe hypoglycemia events but the number of events reported is generally small and effect estimates are 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 3 to 4 RCTs have found statistically significant benefits of CGM in terms of glycemic control. However, the degree of HbA1c reduction and the difference in HbA1c reduction between groups may not be clinically significant. In addition, the small number of RCTs and variability among interventions makes 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 generally have 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 3 RCTs that assessed large-for-gestational age infants as a primary or a secondary outcome did not find a significantly lower rate in women who used CGM. Other outcomes, such as maternal glycemic control and neonatal hypoglycemia, tended not to be significantly improved with CGM. The evidence is insufficient to determine the effects of the technology on health outcomes.

CLINICAL INPUT RECEIVED THROUGH PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society and 4 academic medical centers. Those providing input concurred that this technique, particularly intermittent glucose monitoring, was helpful in a subset of patients with diabetes. Reviewers commented that this monitoring can improve diabetes care by reducing glucose levels (and improving HbA1c) and/or by reducing episodes of hypoglycemia. Reviewers argued that there was persuasive information from case reports to demonstrate the positive impact of intermittent glucose monitoring.

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Association of Clinical Endocrinologists and American College of Endocrinology

In 2016, the American Association of Clinical Endocrinologists and American College of Endocrinology published a consensus statement on outpatient glucose monitoring. Following are their recommendations on CGM:

- Type 1 diabetes, adults: “CGM recommended, especially for patients with history of severe hypoglycemia, hypoglycemia unawareness and to assist in the correction of hyperglycemia in patients not at goal. CGM users must know basics of sensor insertion, calibration and real-time data interpretation.”
- Type 1 diabetes, children: Same as adults, except that more training and follow-up is needed.
- Type 2 diabetes receiving insulin, sulfonylureas, or glinides: “Data on CGM in T2DM [type 2 diabetes mellitus] are limited at this time. Trials assessing the use of CGM in T2DM are ongoing.”

National Institute for Health and Care Excellence

In 2015, the National Institute for Health and Care Excellence released guidelines on diagnosis and management of type I diabetes in adults. The guidelines state:

- “Do not offer real-time continuous glucose monitoring routinely to adults with type 1 diabetes”
- “Consider real-time continuous glucose monitoring for adults with type 1 diabetes who are willing to commit to using it at least 70% of the time and to calibrate it as needed, and
who have any of the following despite optimised use of insulin therapy and conventional blood glucose monitoring:

- More than 1 episode a year of severe hypoglycaemia with no obviously preventable precipitating cause.
- Complete loss of awareness of hypoglycaemia.
- Frequent (more than 2 episodes a week) asymptomatic hypoglycaemia that is causing problems with daily activities.
- Extreme fear of hypoglycaemia.
- Hyperglycaemia (HbA1c level of 75 mmol/mol [9%] or higher) that persists despite testing at least 10 times a day. Continue real-time continuous glucose monitoring only if HbA1c can be sustained at or below.”

American Diabetes Association
In 2014, the American Diabetes Association made the following recommendations concerning continuous glucose monitoring27:

- CGM "in conjunction with intensive insulin regimens can be a useful tool to lower A1c in selected adults (age at least 25 years) with type 1 diabetes." (Level of evidence A)
- "Although the evidence of A1c lowering is less strong in children, teens, and younger adults, CGM may be helpful in those groups. Success correlates with adherence to ongoing use of the device." (Level of evidence C)
- "CGM may be a supplemental tool to SMBG [self-monitoring of blood glucose] in those with hypoglycemic unawareness and/or frequent hypoglycemic episodes." (Level of evidence E)

Endocrine Society
In 2011, the Endocrine Society published a clinical practice guideline developed by a task force that included the following recommendations on continuous glucose monitoring(28):

1.0 Real-time continuous glucose monitoring (RT-CGM) in adult hospital settings
1.1 We recommend against the use of RT-CGM alone for glucose management in the intensive care unit or operating room until further studies provide sufficient evidence for its accuracy and safety in those settings.

2.0 Children and adolescent outpatients
2.1 We recommend that RT-CGM with currently approved devices be used by children and adolescents with type 1 diabetes mellitus who have achieved HbA1c levels below 7.0%.
2.2 We recommend RT-CGM devices be used with children and adolescents with type 1 diabetes who have HbA1c levels 7.0% or higher who are able to use these devices on a nearly daily basis.
2.3 We make no recommendations for or against the use of RT-CGM by children with type 1 diabetes who are less than 8 yr of age.
2.4 We suggest that treatment guidelines regarding use of RT-CGM be provided to patients.
2.5 We suggest the intermittent use of CGM systems designed for short-term retrospective analysis in pediatric patients with diabetes in whom clinicians worry about nocturnal hypoglycemia, dawn phenomenon, and postprandial hyperglycemia; in patients with hypoglycemic unawareness; and in patients experimenting with important changes to their diabetes regimen.
3.0 Adult outpatients
3.1 We recommend that RT-CGM devices be used by adult patients with type 1 diabetes who have HbA1c levels of at least 7.0% and who have demonstrated that they can use these devices on a nearly daily basis.
3.2 We recommend that RT-CGM devices be used by adult patients with type 1 diabetes who have HbA1c levels less than 7.0% and who have demonstrated that they can use these devices on a nearly daily basis.
3.3 We suggest that intermittent use of CGM systems designed for short-term retrospective analysis may be of benefit in adult patients with diabetes to detect nocturnal hypoglycemia, the dawn phenomenon, and postprandial hyperglycemia, and to assist in the management of hypoglycemic unawareness and when significant changes are made to their diabetes regimen.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
The U.S. Preventive Services Task Force has not addressed continuous or intermittent glucose monitoring in patients with diabetes.

CODING
The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS
95250 Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording
95251 Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; interpretation and report
0446T Creation of subcutaneous pocket with insertion of implantable interstitial glucose sensor, including system activation and patient training
0447T Removal of implantable interstitial glucose sensor from subcutaneous pocket via incision
0448T Removal of implantable interstitial glucose sensor with creation of subcutaneous pocket at different anatomic site and insertion of new implantable sensor, including system activation
A9276 Sensor; invasive (e.g., subcutaneous), disposable, for use with interstitial continuous glucose monitoring system, 1 unit = 1 day supply
A9277 Transmitter; external, for use with interstitial continuous glucose monitoring system
A9278 Receiver (monitor); external, for use with interstitial continuous glucose monitoring system
K0553 Supply allowance for therapeutic continuous glucose monitor (CGM), includes all supplies and accessories, 1 month supply = 1 Unit of Service
K0554 Receiver (monitor), dedicated, for use with therapeutic continuous glucose monitor system
S1030 Continuous noninvasive glucose monitoring device, purchase (for physician interpretation of data, use CPT code)
S1031 Continuous noninvasive glucose monitoring device, rental, including sensor, sensor replacement, and download to monitor (for physician interpretation of data, use CPT code)

**ICD-9 Diagnoses**

250.01 Diabetes mellitus without mention of complication, type I (juvenile type), not stated as uncontrolled
250.03 Diabetes mellitus without mention of complication, type I (juvenile type), uncontrolled
250.11 Diabetes with ketoacidosis, type I (juvenile type), not stated as uncontrolled
250.13 Diabetes with ketoacidosis, type I (juvenile type), uncontrolled
250.21 Diabetes with hypertension, type I (juvenile type), not stated as uncontrolled
250.23 Diabetes with hypertension, type I (juvenile type), uncontrolled
250.31 Diabetes with other coma, type I (juvenile type), not stated as uncontrolled
250.33 Diabetes with other coma, type I (juvenile type), uncontrolled
250.41 Diabetes with renal manifestations, type I (juvenile type), not stated as uncontrolled
250.43 Diabetes with renal manifestations, type I (juvenile type), uncontrolled
250.51 Diabetes with ophthalmic manifestations, type I (juvenile type), not stated as uncontrolled
250.53 Diabetes with ophthalmic manifestations, type I (juvenile type), uncontrolled
250.61 Diabetes with neurologic manifestations, type I (juvenile type), not stated as uncontrolled
250.63 Diabetes with neurologic manifestations, type I (juvenile type), uncontrolled
250.71 Diabetes with peripheral circulatory disorders, type I (juvenile type), not stated as uncontrolled
250.73 Diabetes with peripheral circulatory disorders, type I (juvenile type), uncontrolled
250.81 Diabetes with other specified manifestations, type I (juvenile type), not stated as uncontrolled
250.83 Diabetes with other specified manifestations, type I (juvenile type), uncontrolled
250.91 Diabetes with other unspecified complications, type I (juvenile type), not stated as uncontrolled
250.93 Diabetes with other unspecified complications, type I (juvenile type), uncontrolled
648.80 Abnormal glucose tolerance (gestational diabetes); unspecified as to episode of care or not applicable
648.83 Abnormal glucose tolerance (gestational diabetes); antepartum condition or complication

**ICD-10 Diagnoses**

E10.10 Type 1 diabetes mellitus with ketoacidosis without coma
E10.11 Type 1 diabetes mellitus with ketoacidosis with coma
E10.21 Type 1 diabetes mellitus with diabetic nephropathy
E10.22 Type 1 diabetes mellitus with diabetic chronic kidney disease
E10.29 Type 1 diabetes mellitus with other diabetic kidney complication
E10.311 Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10.319  Type 1 diabetes mellitus with unspecified diabetic retinopathy without macular edema
E10.3211 Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E10.3212 Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E10.3213 Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3291 Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye
E10.3292 Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye
E10.3293 Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral
E10.3311 Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E10.3312 Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E10.3313 Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3391 Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye
E10.3392 Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye
E10.3393 Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral
E10.3411 Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E10.3412 Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E10.3413 Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3491 Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye
E10.3492 Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye
E10.3493 Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral
E10.3511 Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E10.3512 Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E10.3513 Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E10.3521 Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
E10.3522 Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E10.3523</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral</td>
</tr>
<tr>
<td>E10.3531</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye</td>
</tr>
<tr>
<td>E10.3532</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye</td>
</tr>
<tr>
<td>E10.3533</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral</td>
</tr>
<tr>
<td>E10.3541</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye</td>
</tr>
<tr>
<td>E10.3542</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye</td>
</tr>
<tr>
<td>E10.3543</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral</td>
</tr>
<tr>
<td>E10.3551</td>
<td>Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye</td>
</tr>
<tr>
<td>E10.3552</td>
<td>Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye</td>
</tr>
<tr>
<td>E10.3553</td>
<td>Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral</td>
</tr>
<tr>
<td>E10.3591</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye</td>
</tr>
<tr>
<td>E10.3592</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye</td>
</tr>
<tr>
<td>E10.3593</td>
<td>Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral</td>
</tr>
<tr>
<td>E10.36</td>
<td>Type 1 diabetes mellitus with diabetic cataract</td>
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<tr>
<td>E10.37X1</td>
<td>Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye</td>
</tr>
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<td>E10.37X2</td>
<td>Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye</td>
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<tr>
<td>E10.37X3</td>
<td>Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral</td>
</tr>
<tr>
<td>E10.39</td>
<td>Type 1 diabetes mellitus with other diabetic ophthalmic complication</td>
</tr>
<tr>
<td>E10.40</td>
<td>Type 1 diabetes mellitus with diabetic neuropathy, unspecified</td>
</tr>
<tr>
<td>E10.41</td>
<td>Type 1 diabetes mellitus with diabetic mononeuropathy</td>
</tr>
<tr>
<td>E10.42</td>
<td>Type 1 diabetes mellitus with diabetic polyneuropathy</td>
</tr>
<tr>
<td>E10.43</td>
<td>Type 1 diabetes mellitus with diabetic autonomic (poly)neuropathy</td>
</tr>
<tr>
<td>E10.44</td>
<td>Type 1 diabetes mellitus with diabetic amyotrophy</td>
</tr>
<tr>
<td>E10.49</td>
<td>Type 1 diabetes mellitus with other diabetic neurological complication</td>
</tr>
<tr>
<td>E10.51</td>
<td>Type 1 diabetes mellitus with diabetic peripheral angiopathy without gangrene</td>
</tr>
<tr>
<td>E10.52</td>
<td>Type 1 diabetes mellitus with diabetic peripheral angiopathy with gangrene</td>
</tr>
<tr>
<td>E10.59</td>
<td>Type 1 diabetes mellitus with other circulatory complications</td>
</tr>
<tr>
<td>E10.610</td>
<td>Type 1 diabetes mellitus with diabetic neuropathic arthropathy</td>
</tr>
<tr>
<td>E10.618</td>
<td>Type 1 diabetes mellitus with other diabetic arthropathy</td>
</tr>
<tr>
<td>E10.620</td>
<td>Type 1 diabetes mellitus with diabetic dermatitis</td>
</tr>
<tr>
<td>E10.621</td>
<td>Type 1 diabetes mellitus with foot ulcer</td>
</tr>
<tr>
<td>E10.622</td>
<td>Type 1 diabetes mellitus with other skin ulcer</td>
</tr>
<tr>
<td>E10.628</td>
<td>Type 1 diabetes mellitus with other skin complications</td>
</tr>
<tr>
<td>E10.630</td>
<td>Type 1 diabetes mellitus with periodontal disease</td>
</tr>
<tr>
<td>E10.638</td>
<td>Type 1 diabetes mellitus with other oral complications</td>
</tr>
</tbody>
</table>
E10.641  Type 1 diabetes mellitus with hypoglycemia with coma
E10.649  Type 1 diabetes mellitus with hypoglycemia without coma
E10.65  Type 1 diabetes mellitus with hyperglycemia
E10.69  Type 1 diabetes mellitus with other specified complication
E10.8   Type 1 diabetes mellitus with unspecified complications
E10.9   Type 1 diabetes mellitus without complications
O24.410 Gestational diabetes mellitus in pregnancy, diet controlled
O24.414 Gestational diabetes mellitus in pregnancy, insulin controlled
O24.415 Gestational diabetes mellitus in pregnancy, controlled by oral hypoglycemic drugs
O24.419 Gestational diabetes mellitus in pregnancy, unspecified control
O99.810 Abnormal glucose complicating pregnancy

**REVISIONS**

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>01-26-2004</td>
<td>Deleted “Certain diabetic and newly pregnant or who are about to conceive” and “Patients who are about to start insulin for the first time using an insulin pump regimen”</td>
</tr>
<tr>
<td></td>
<td>Added “Suboptimal glycemic control as reflected by a glycohemoglobin (HbA1c) value of greater than 7.0 percent.”</td>
</tr>
<tr>
<td></td>
<td>Added “Repeat testing for Continuous Glucose Monitoring System® (CGMS®):</td>
</tr>
<tr>
<td></td>
<td>a. Prior Approval is recommended;  and</td>
</tr>
<tr>
<td></td>
<td>b. Patient is compliant on a prescribed intensive insulin program/therapy; and</td>
</tr>
<tr>
<td></td>
<td>c. May occur four to six weeks following the initial study.”</td>
</tr>
<tr>
<td></td>
<td>Added “Use of noninvasive continuous glucose monitoring devices (eg Gluco Watch Biographer®) and related supplies is considered experimental/investigational for all indications.”</td>
</tr>
<tr>
<td>04-21-2005</td>
<td>Added the definition of “intensive insulin therapy”.</td>
</tr>
<tr>
<td></td>
<td>Added, “The use of combined insulin, such as 70/30 insulin did not meet the criteria for “program involvement’ of multiple daily injections.”</td>
</tr>
<tr>
<td>11-02-2006</td>
<td>In “Description” section, deleted the paragraph starting with “The GlucoWatch is similar in appearance to a wristwatch that is worn on the inner or” as recommended by the Medical Director.</td>
</tr>
<tr>
<td>effective</td>
<td></td>
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<tr>
<td>01-02-2007</td>
<td>In “Description” section, deleted the paragraph starting with “Although the noninvasiveness is an attractive quality of the device, it should be…” as recommended by the Medical Director.</td>
</tr>
<tr>
<td></td>
<td>In “Description” section, deleted “For calibration purposes, the manufacturer recommends that the patient enter the results of 4 fingerstick blood glucose measurements per day into the monitor. For the Guardian CGMS, it is recommended that the device be calibrated with fingerstick blood glucose levels every 12 hours at a minimum. The Guardian CGMS does feature an audible alarm that sounds when glucose levels become too high or too low per parameters set by the patient and physician.” as recommended by the Medical Director.</td>
</tr>
<tr>
<td></td>
<td>In “Description” section, deleted the paragraph starting with “The definition of ‘Intensive Insulin Therapy’ is the use of an insulin regimen that…” as recommended by the Medical Director.</td>
</tr>
<tr>
<td></td>
<td>In “Policy” section, first paragraph, added “(multiple daily injections (MDI) of 4-5 injections of insulin per day or insulin pump).” as recommended by the Medical Director.</td>
</tr>
<tr>
<td></td>
<td>In “Policy” section, deleted “and one of the following conditions have been met:” and the “or” at the end of #1, #2, and #3 sentences per November MAC.</td>
</tr>
<tr>
<td></td>
<td>In “Policy” section, added to the end of the opening sentence “The following conditions will be considered to determine medical necessity:” per November MAC.</td>
</tr>
<tr>
<td></td>
<td>In “Policy” section, added “Unexplained” to the beginning of #3 and #4 per November MAC.</td>
</tr>
</tbody>
</table>
Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid

In “Documentation” section, deleted “Program Involvement (all required):” as recommended by the Medical Director.

In “Documentation” section, deleted #2 “Basal insulin usually involves “Ultralente” and “Lantus” insulin.” as recommended by the Medical Director.

In “Documentation” section, deleted #3 “Bolus insulin (insulin analogue) usually involves “Humalog” or “Novolog” insulin.” as recommended by the Medical Director.

In “Coding” Covered Diagnosis, deleted ICD-9 codes (for type II) 250.00, 250.02, 250.10, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.50, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, and 250.92 as recommended by the Medical Director.

In “Reference” Government Agency; Medical Society; and Other Authoritative Publications section, added new #3 through #7.

07-17-2007
In Policy section:
- Added clarification to policy that continuous glucose monitoring system is limited to 72 hours. Extended use beyond 72 hours is considered patient deluxe, patient responsibility/non-covered.
In Coding section:
- Removed code 99091.

01-01-2008
In Coding section:
- Added codes and nomenclature for A9276, A9277, A9278.

09-03-2008
In Coding section:
- Added codes and nomenclature for S1030, S1031.
- Corrected nomenclature for 95250.
In Policy section:
Revised wording from "requires prior approval" to "prior approval is encouraged".

09-09-2009
In Header:
- Revised title from Continuous Glucose Monitoring System (CGMS) to Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid.
In Description section:
- Updated wording.
In Policy section:
- Updated wording on intermittent monitoring, no change in policy position.
- Added indication of:
Continuous, ie, 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 I diabetes who have recurrent, unexplained, severe, symptomatic (generally blood glucose levels less than 50 mg/dl) hypoglycemia for whom hypoglycemia puts the patient or others at risk; or
- Patients with type I diabetes who have recurrent diabetic ketoacidosis (DKA) requiring emergency room visits and admissions.
- Patients with type I diabetes who are pregnant whose diabetes is poorly controlled. Poorly controlled type I diabetes 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.

Added Rationale section.
In Coding section:
- Added CPT/HCPCS codes: 99091, A9278
- Added Diagnoses codes: 648.80, 648.83
<table>
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<th>Date</th>
<th>Updates</th>
</tr>
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<tbody>
<tr>
<td>03-25-2011</td>
<td>In Policy Guidelines section:&lt;br&gt;• Added &quot;or multiple daily injections&quot; to read &quot;Best practices in diabetes control for patients with type I diabetes include compliance with a regimen of 4 or more fingersticks each day and the use of an insulin pump, or multiple daily injections.&quot;</td>
</tr>
<tr>
<td>10-04-2013</td>
<td>Updated Description section. In Policy section:&lt;br&gt;• Formatted medical policy language.&lt;br&gt;• In Item C, #1, removed &quot;symptomatic&quot; to read &quot;Patients with type I diabetes who have recurrent, unexplained, severe (generally blood glucose levels less than 50 mg/dl) hypoglycemia...&quot;&lt;br&gt;• In Item D, inserted &quot;experimental/&quot; to read &quot;Other uses of continuous monitoring of glucose levels in interstitial fluid as a technique of diabetic monitoring are considered experimental / investigational.&quot;&lt;br&gt;• Added Item E, &quot;Use of artificial pancreas system, including but not limited to closed-loop monitoring devices with low-glucose suspend (LGS) features, are considered experimental / investigational.&quot;&lt;br&gt;• In Policy Guidelines, add the following statements:&lt;br&gt;  o &quot;Several insulin pump systems (eg, Omnipod Insulin Management System, Paradigm REAL-Time System) have a built-in continuous glucose monitor (CGM). This policy is evaluating the CGM-device only; the policy does not evaluate insulin pumps. In the case of insulin pumps systems with built-in CGM and low glucose feature, the CGM device and the low glucose suspend feature are evaluated in the policy, not the insulin pump.&quot;&lt;br&gt;  o &quot;The strongest evidence exists for use of the 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.&quot;</td>
</tr>
<tr>
<td>03-06-2015</td>
<td>Updated Description section. In Policy section:&lt;br&gt;• Removed Item E, &quot;Use of an artificial pancreas system, including but not limited to closed loop monitoring devices with low glucose suspend (LGS) features, are considered experimental/investigational.&quot;</td>
</tr>
<tr>
<td>08-04-2016</td>
<td>Updated Description section. In Policy Guidelines section:&lt;br&gt;• In Item #2, removed &quot;type I&quot; and added &quot;mellitus&quot; to read, &quot;Best practices in diabetes control for patients with diabetes mellitus include compliance with a regimen ...&quot;&lt;br&gt;• In Item #3, added &quot;mellitus&quot; to read, &quot;Women with type I diabetes mellitus who are present or about to become ...&quot;&lt;br&gt;• In Item #4, removed &quot;four weeks depending on the patient's level of diabetes control and medical necessity&quot;, and added &quot;a subsequent time depending on the patient's level of diabetes control&quot;, to read, &quot;Intermittent monitoring is generally conducted in 72-hour periods. It may be repeated at a subsequent time depending on the patient's level of diabetes control.&quot;</td>
</tr>
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</table>
In Policy section:

- In Policy Guidelines Item 1, removed "Omnipod Insulin Management System," to read
  "Several insulin pump systems (e.g., Paradigm® REAL-Time System) have a built-in
  continuous glucose monitor (CGM). This policy is evaluating the CGM-device only; the
  policy does not evaluate insulin pumps. In the case of insulin pump systems with a
  built-in CGM and low glucose suspend (LGS) feature, the CGM device and the low
  glucose suspend feature are evaluated in the policy, not the insulin pump."

Updated Rationale section.

Updated References section.

<table>
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<tr>
<td>07-01-2017</td>
<td>Added CPT codes: 0446T, 0447T, 0448T.</td>
</tr>
</tbody>
</table>

REFERENCES

3. Blue Cross and Blue Shield Technology Evaluation Center (TEC). Use of intermittent or continuous interstitial fluid glucose monitoring in patients with diabetes mellitus. TEC Assessments. 2003;Volume 18, Tab 16. PMID


Other References
2. Blue Cross and Blue Shield of Kansas Internal Medicine Liaison Committee, August 2008; August 2009; August 2013; August 2014.
3. Blue Cross and Blue Shield of Kansas Family Practice Liaison Committee, July 2009.
4. Blue Cross and Blue Shield of Kansas Consent Ballot, June 2009: Family Practice Liaison Committee; Internal Medicine Liaison Committee; Pediatric Liaison Committee.