**Medical Policy**

**Title:** Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid

**Professional**
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Current Effective Date: September 1, 2017

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<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals: • With type 1 diabetes who are willing and able to use the device, and have adequate medical supervision</td>
<td>Interventions of interest are: • Long-term (continuous) glucose monitoring</td>
<td>Comparators of interest are: • Self-monitoring of blood glucose</td>
<td>Relevant outcomes include: • Symptoms • Morbid events • Quality of life • Treatment-related morbidity</td>
</tr>
</tbody>
</table>
### DESCRIPTION

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.

### OBJECTIVE

The objective of this policy is to evaluate whether continuous glucose monitoring improves health outcomes in patients with diabetes.

### 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 HgA1c 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 1 diabetics in decreasing microvascular complications. The impact of tight control on type 2 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. 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 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 to measure glucose values automatically 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 (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\(^\circ\)) (MiniMed), which uses an implanted temporary sensor in the subcutaneous tissues, and the GlucoWatch G2\(^\circ\) 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 stored data for download and retrospective analysis by a clinician. With currently available devices, the intervals at which interstitial glucose is measured range from every 1-2 minutes to 5 minutes and most provide measurements in real-time directly to patients. 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 (see Table 1):
Continuous or Intermittent Monitoring of Glucose in Interstitial Fluid

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

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Approval</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous Glucose Monitoring System (CGMS®)</td>
<td>MiniMed</td>
<td>1999</td>
<td>3-d use in physician's office</td>
</tr>
<tr>
<td>GlucoWatch G2® Biographer⁵</td>
<td></td>
<td>2001</td>
<td></td>
</tr>
<tr>
<td>Guardian®-RT (Real-Time) CGMS</td>
<td>MiniMed (now Medtronic)</td>
<td>2005</td>
<td></td>
</tr>
<tr>
<td>Dexcom® STS CGMS system</td>
<td>Dexcom</td>
<td>2006</td>
<td></td>
</tr>
<tr>
<td>Paradigm® REAL-Time System (second generation called Paradigm Revel System)</td>
<td>MiniMed (now Medtronic)</td>
<td>2006</td>
<td>System integrates a CGM with a Paradigm insulin pump</td>
</tr>
<tr>
<td>FreeStyle Navigator® CGM System</td>
<td>Abbott</td>
<td>2008</td>
<td></td>
</tr>
<tr>
<td>Dexcom® G4 Platinum</td>
<td>Dexcom</td>
<td>2012</td>
<td>Adults ≥18 y; can be worn for up to 7 d;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2014</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Expanded use to include patients with diabetes 2-17 y</td>
</tr>
<tr>
<td>Dexcom® G5 Mobile CGM</td>
<td></td>
<td>2016</td>
<td>Replacement for fingerstick blood glucose testing in patients ≥2 y. System requires at least 2 daily fingerstick tests for calibration purposes, but additional fingersticks are not necessary because treatment decisions can be made based on device readings.³</td>
</tr>
</tbody>
</table>

CGM: continuous glucose monitoring.

⁵ Neither the GlucoWatch nor the autosensors have been available since July 2008.

³ As a supplement to the G4 premarketing approval.

FDA product codes: MDS, PQF.

POLICY

A. Intermittent monitoring, ie, up to 72 hours, of glucose levels in interstitial fluid may be considered **medically necessary** in patients with type 1 diabetes whose diabetes is poorly controlled, despite current use of best practices (see Policy Guidelines). Poorly controlled type 1 diabetes 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 1 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 1 diabetes 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

2. Patients with type 1 diabetes who have recurrent diabetic ketoacidosis (DKA) requiring emergency room visits and admissions; or

3. Patients with poorly controlled type 1 diabetes who are pregnant. Poorly controlled type 1 diabetes includes unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis; or

4. 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.

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.

**Policy Guidelines**

1. Several insulin pump systems (eg, 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 this policy, not the insulin pump.

2. Best practices in diabetes control include compliance with a regimen of 4 or more fingersticks each day and use of an insulin pump. 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 1 diabetes 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.
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.

6. 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 (ie, long-term) monitoring.

RATIONALE
A TEC Assessment was published in 2003. The most recent literature review was performed for the period through April 25, 2017. 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.

This policy combines discussion of the first 2 indications because several of the systematic reviews and RCTs provided information relevant to both indications. Separate section summaries address each indication.

CGM Devices for Long-Term Use
Systematic Reviews
A number of systematic reviews and meta-analyses of RCTs evaluating CGM for long-term, daily use in treating type 1 diabetes have been published. These systematic reviews have focused on slightly different populations, and some did not separate long-term CGM from intermittent glucose monitoring. The most recent meta-analysis, which was also the only analysis that used individual patient data, was published by Benkhadra et al in 2017. The meta-analysis evaluated data from 11 RCTs that enrolled patients with type 1 diabetes and compared real-time CGM to a control intervention. Studies in which patients used insulin pumps or received multiple daily insulin injections were included. Reviewers contacted corresponding study authors requesting individual patient data; data were not obtained for 1 trial. Mean baseline hemoglobin A1c (HbA1c) levels were 8.2% in adults and 8.3% in children and adolescents. The overall risk of bias in the studies was judged to be moderate. In pooled analyses, there was a statistically significantly
greater decrease in HbA1c levels with real-time CGM vs control conditions. Overall, the degree of difference between groups was 0.26%. In subgroup analyses by age, there was significantly greater change in HbA1c levels among individuals 15 years and older, but not among the younger age groups. There were no significant differences between groups in the time spent in hypoglycemia or in the incidence of hypoglycemic events. Key findings are shown in Table 2.

**Table 2. Main Findings From a 2017 Individual Patient Data Meta-Analysis on Real-Time CGM**

<table>
<thead>
<tr>
<th>No. of Trials</th>
<th>N</th>
<th>Outcomes</th>
<th>Point Value</th>
<th>95% Confidence Intervals</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in HbA1c levels, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1371</td>
<td>Overall</td>
<td>-0.258</td>
<td>0.464 to -0.052</td>
<td>0.014</td>
</tr>
<tr>
<td>7</td>
<td>902</td>
<td>Age &gt;15 y</td>
<td>-0.356</td>
<td>0.551 to -0.160</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>7</td>
<td>178</td>
<td>Age 13-15 y</td>
<td>-0.039</td>
<td>-0.320 to 0.242</td>
<td>0.787</td>
</tr>
<tr>
<td>7</td>
<td>291</td>
<td>Age ≤12 y</td>
<td>-0.047</td>
<td>0.217 to 0.124</td>
<td>0.592</td>
</tr>
<tr>
<td><strong>Time spent in hypoglycemia &lt;60 mg/dL, min</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>706</td>
<td>Overall</td>
<td>-8.549</td>
<td>-31.083 to 13.985</td>
<td>0.457</td>
</tr>
<tr>
<td>4</td>
<td>467</td>
<td>Age &gt;15 y</td>
<td>-8.095</td>
<td>-32.615 to 16.425</td>
<td>0.518</td>
</tr>
<tr>
<td>3</td>
<td>109</td>
<td>Age 13-15 y</td>
<td>-13.966</td>
<td>31.782 to 3.852</td>
<td>0.124</td>
</tr>
<tr>
<td>3</td>
<td>130</td>
<td>Age ≤12 y</td>
<td>-9.366</td>
<td>19.898 to 1.167</td>
<td>0.081</td>
</tr>
<tr>
<td><strong>Incidence of hypoglycemic events &lt;70 mg/dL, mean no. events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>351</td>
<td>Overall</td>
<td>0.051</td>
<td>-0.314 to 0.416</td>
<td>0.785</td>
</tr>
<tr>
<td>3</td>
<td>277</td>
<td>Age &gt;15 y</td>
<td>-0.074</td>
<td>-0.517 to 0.368</td>
<td>0.742</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>Age 13-15 y</td>
<td>0.536</td>
<td>0.243 to 1.316</td>
<td>0.177</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>Age ≤12 y</td>
<td>0.392</td>
<td>0.070 to 0.854</td>
<td>0.097</td>
</tr>
</tbody>
</table>

CGM: continuous glucose monitoring; HbA1c: hemoglobin A1c.

A systematic review by Yeoh et al (2015) addressed a broad range of interventions to restore hypoglycemia awareness in adults with type 1 diabetes (ie, educational, technologic, and pharmacologic interventions) and did not identify any RCTs focusing on CGM for hypoglycemia unawareness.10 Earlier meta-analyses of glucose monitoring devices for type 1 diabetes tended to combine studies of intermittent glucose monitoring with studies of long-term CGM. Several reported separate subgroup analyses for long-term CGM. A 2012 Cochrane review of CGM in type 1 diabetes in adults and children included RCTs comparing CGM with conventional self-monitored blood glucose (SMBG).7 In pooled analysis (6 studies; n=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 for 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, n=154 patients; MD change, 0.1; 95% CI, -0.5 to 0.7). In a meta-analysis of 4 RCTs (n=689 patients), there was no significant difference in the 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. 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 systematic review of RCTs on CGM included trials conducted in adults and children with type 1 diabetes.9 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 vs SMBG (standardized mean difference, -0.32; 95% CI, -0.52 to -0.13). In 5 studies reporting the percentage of patients with severe hypoglycemic episodes, there were no differences in the percentage of patients with severe hypoglycemic episodes using CGM and SMBG in any of them.

**Randomized Controlled Trials**

Recent RCTs not included in the meta-analyses are described next.

Van Beers et al (2016) published a crossover RCT comparing CGM with SMBG and focusing on patients with impaired hypoglycemia awareness. Eligible patients were 18 to 75 years old, were treated with insulin infusion pumps or multiple daily insulin injections, undertook at least 3 SMBG measurements per day, and had impaired awareness of hypoglycemia (ie, Gold score ≥4). The trial used an artificial pancreas device system without using the low glucose suspend feature. After a 6-week run-in phase (during which patients received education about diabetes management), 52 patients received both 16 weeks of CGM and 16 weeks of SMBG, in random order. There was a 12-week washout period between interventions. All patients were included in the primary intention-to-treat analysis. Six patients withdrew from the study early.

The primary outcome, time spent in normoglycemia (4-10 mmol/L), was significantly higher in the CGM phase than in the SMBG phase. The percentage of time spent in normoglycemia was 65.0% in the CGM phase and 55.4% in the SMBG group (MD=9.6%; p<0.001). The sequence allocation did not have an effect on the primary end point. Most other CGM-derived outcomes (eg, number and duration of nocturnal hypoglycemia events) also significantly favored the CGM group. The total number of severe hypoglycemic events (ie, those needing third-party assistance) was 14 in the CGM phase and 34 in the SMBG phase, which differed significantly between groups (p=0.033). The number of patients with 1 or more severe hypoglycemic event during the intervention period, however, did not differ significantly between phases 10 in the CGM phase and 18 in the SMBG phase (p=0.062). HbA1c outcomes did not differ significantly; eg, change in HbA1c levels from baseline was -0.1% in both phases (p=0.449). In terms of hypoglycemia awareness, one of 4 variables, Gold score at the study end point differed significantly (mean, 4.6 for the CGM phase vs 5.0 for the SMBG phase, p=0.035); 3 other variables related to hypoglycemia awareness did not differ between groups.

Two 2017 RCTs evaluated long-term CGM in patients with type 1 diabetes treated with multiple daily insulin injections. Both trials used the Dexcom G4 CGM device. Lind et al (2017) reported on a crossover study with 142 adults ages 18 and older who had baseline HbA1c levels of 7.5% or higher (mean baseline HbA1c level, ≈8.5%). There was a 6-week run-in period using a CGM device with masked data and patients were excluded from further participation if they did not believe they would use the device more than 80% of the time or did not perform an adequate
number of calibrations during the run-in period. Enrolled patients underwent 26-week treatment periods with a CGM device and conventional therapy using SMBG, in random order. There was a 17-week washout period between intervention phases. The primary end point was the difference in HbA1c levels at the end of each treatment period. Mean HbA1c levels were 7.9% during CGM use and 8.4% during conventional therapy (mean difference, -0.4%; p<0.01). There were a large number of secondary end points. A portion of them were prespecified and analyses took into consideration the statistical impact of multiple comparisons; the remaining secondary outcomes were considered descriptive and p values were not reported. Among the prespecified secondary outcomes, treatment satisfaction (measured by the Diabetes Treatment Satisfaction Questionnaire) was significantly higher in the CGM phase than in the conventional treatment phase (p<0.001). Hypoglycemia outcomes were secondary descriptive outcomes. There was 1 (0.7%) severe hypoglycemic event during the CGM phase and 5 (3.5%) events during conventional therapy. The percentage of time with hypoglycemia (<70 mmol/L) was 2.8% during CGM treatment and 4.8% during conventional therapy.

In the second study, Beck et al (2017) randomized 158 patients on a 2:1 basis to 24 weeks of CGM (n=105) or to usual care (n=53). The trial included patients with type 1 diabetes who were ages 25 or older and had baseline HbA1c levels between 7.5% and 10%. Before randomization, patients underwent a 2-week period using a CGM system (without seeing data from the CGM) to ensure compliance. To be eligible, patients had to wear the CGM on at least 85% of days, calibrate the device at least twice daily and perform SMBG at least 3 times daily. The primary outcome (change in HbA1c levels at 24 weeks) was 1.0% in the CGM group and 0.4% in the usual care group (p<0.001), with a between-group difference of 0.6%. Prespecified secondary outcomes on the proportion of patients below a glycemic threshold at 24 weeks also favored the CGM group. The proportion of patients with HbA1c levels less than 7.0% was 18 (18%) in the CGM group and 2 (4%) in the control group (p=0.01). The proportion of patients with HbA1c levels less than 7.5% was 39 (38%) in the CGM group and 6 (11%) in the control group (p<0.001). Moreover, prespecified secondary outcomes related to hypoglycemia also differed significantly between groups, favoring the CGM group. The time spent in hypoglycemia less than 70 mg/dL was 43 minutes per day in the CGM group and 80 minutes per day in the usual care group (p=0.002). Comparable numbers for time spent at less than 50 mg/dL were 6 minutes per day in the CGM group and 20 minutes per day in the usual care group (p=0.001).

Section Summary: CGM Devices for Long-Term Use in Type 1 Diabetes
Numerous RCTs and several systematic reviews of RCTs have evaluated CGM in patients with type 1 diabetes. A 2017 individual patient data analysis, using data from 11 RCTs, found that reduction in HbA1c levels was significantly greater with real-time CGM compared with a control intervention. In addition, a 2012 meta-analysis of 6 RCTs found a significantly larger decline in HbA1c levels at 6 months in CGM users than the SMBG group. There are few studies beyond 6 months. Two recent 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 HbA1c levels than previous studies. Reductions were 0.4% and 0.6%, respectively, compared with approximately 0.2% to 0.3% in previous analyses. One of the 2 RCTs prespecified hypoglycemia-related outcomes, and time spent in hypoglycemia was significantly less in the CGM group.
Section Summary: CGM Devices for Long-Term Use in Type 1 Diabetes and Impaired Hypoglycemia Awareness and/or History of Recurrent Unexplained Severe Hypoglycemia

Although meta-analyses of RCTs on CGM have generally not shown a significant difference in hypoglycemia outcomes between CGM and SMBG, those RCTs included a variety of patients and did not focus in patients at highest risk of hypoglycemia. A 2016 crossover RCT 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 SMBG. Findings from this trial can be extrapolated to a related group of patients at increased risk of severe hypoglycemia—those patients with a history of recurrent, severe unexplained hypoglycemia.

Glucose Monitoring Devices for Short-Term (Intermittent) Use

Meta-analyses of glucose monitoring devices for type 1 diabetes tend 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 have included additional interventions to optimize glucose control (eg, education, 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 HbA1c 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 HbA1c 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; it evaluated whether use of the additional information provided by minimally invasive glucose monitors improved glucose control in patients with poorly controlled insulin-requiring diabetes. This 4-arm RCT was conducted at secondary care diabetes clinics in 4 hospitals in England. This trial enrolled 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. Most (57%) participants had type 1 diabetes (41% had type 2 diabetes, 2% were classified as “other”). Participants had to have 2 HbA1c 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 trial). 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 trial of unselected patients, glucose monitoring (CGMS on an intermittent basis) did not lead to improved clinical outcomes.

Section Summary: Glucose Monitoring Devices for Short-Term (Intermittent) Use in Type 1 Diabetes

For short-term (intermittent) monitoring of type 1 diabetes, there are few RCTs and systematic reviews. Some trials have reported improvements in glucose control for the intermittent monitoring group, but limitations in this body of evidence 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.

Type 2 Diabetes

Two systematic reviews (previously described) also reported on the efficacy of CGM in patients with type 2 diabetes. Gandhi et al (2011) identified 3 RCTs studying patients with type 2 diabetes (1 study included both types of diabetes).6 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 trials 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.8 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 HbA1c levels than SMBG. The pooled mean difference in HbA1c 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.

Ehhardt and colleagues published 2 studies (2011, 2012) reporting on the largest sample size (N=100) in the Poolsup systematic review (accounting for 45% of the weight in the pooled analysis of HbA1c levels).17,18 The trial evaluated intermittent use of a CGM device in adults with type 2 diabetes treated with diet/exercise and/or glycemia-lowering medications but not prandial insulin who had an initial HbA1c level of at least 7% but not more than 12%. The study compared real-time CGM 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 HbA1c levels. Mean (SD) HbA1c 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. During the study, the reduction in HbA1c levels was significantly greater in the CGM group 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 for both groups. The mean proportions 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 HbA1c levels between 6.9% and 11.0% during the previous 3 months, with HbA1c fluctuations within 0.5%. All patients conducted SMBG and used CGM devices that do not have data available in real-time (ie, data are viewed retrospectively by physicians). Devices were used 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 HbA1c levels from baseline, which did not differ significantly between groups at the end of the trial, between the first and second visits, or between the second and third visits. HbA1c levels changed little in either group. In the intervention group, the mean (SD) baseline HbA1c level was 8.2% (1.2%) and the mean final HbA1c 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 on 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 assessing CGM in patients with type 2 diabetes than in 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 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 make 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 CGMs that do not have data available in real-time; the remaining 4 studies used real-time CGM. Reviewers did not pool study findings; they concluded that the evidence was 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 included the intensive SMBG routine in both groups and the relatively low compliance rate (64%) in the CGM group.

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, Wei et al (2016) published an RCT on CGM evaluating 120 women with gestational diabetes at 24 to 28 weeks. Patients were allocated to prenatal care plus CGM (n=58) or to 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 use of 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 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.

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 A1c (HbA1c) 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 HbA1c levels than previous studies. One of the 2 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 HbA1c 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 3 to 4 RCTs have found statistically significant benefits from 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 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 3 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.

**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.24 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 1 diabetes in adults.25 The guidelines state:

1.6.21 “Do not offer real-time continuous glucose monitoring routinely to adults with type 1
diabetes”

1.6.22 “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
The 2017 American Diabetes Association position statement on diabetes includes the following recommendations on CGM (see Table 3).

Table 3. Recommendations on Diabetes Care

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>“When used properly, continuous glucose monitoring (CGM) in conjunction with intensive insulin regimens is a useful tool to lower A1C in selected adults (aged ≥25 years) with type 1 diabetes.”</td>
<td>A</td>
</tr>
<tr>
<td>“Although the evidence for A1C lowering is less strong in children, teens, and younger adults, CGM may be helpful in these groups. Success correlates with adherence to ongoing use of the device.”</td>
<td>B</td>
</tr>
<tr>
<td>“CGM may be a useful tool in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes.”</td>
<td>C</td>
</tr>
</tbody>
</table>

LOE: level of evidence.

a LOE: A: clear evidence from well-conducted, generalizable RCTs that are adequately powered; B: supportive evidence from well-controlled cohort studies; C: supportive evidence from poorly controlled or uncontrolled studies. The Association also recommended that physicians assess individual readiness prior to prescribing CGM and that education, training, and support were needed for optimal CGM device implementation.

Endocrine Society
In 2016, the Endocrine Society published clinical practice guidelines that included the following recommendations on CGM:

6. “Real-time continuous glucose monitors in adult outpatients
   6.1 We recommend real-time continuous glucose monitoring (RT-CGM) devices for adult patients with T1DM [type 1 diabetes mellitus] who have A1C levels above target and who are willing and able to use these devices on a nearly daily basis.
   6.2 We recommend RT-CGM devices for adult patients with well-controlled T1DM who are willing and able to use these devices on a nearly daily basis.
   Use of continuous glucose monitoring in adults with type 2 diabetes mellitus
   6.3 We suggest short-term, intermittent RT-CGM use in adult patients with T2DM (not on prandial insulin) who have A1C levels ≥7% and are willing and able to use the device.”

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 4.

Table 4. Summary of Key Trials

<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>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></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.
a Denotes industry-sponsored or cosponsored trial.
# 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

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

## ICD-9 Diagnoses

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>250.01</td>
<td>Diabetes mellitus without mention of complication, type I (juvenile type), not stated as uncontrolled</td>
</tr>
<tr>
<td>250.03</td>
<td>Diabetes mellitus without mention of complication, type I (juvenile type), uncontrolled</td>
</tr>
<tr>
<td>250.11</td>
<td>Diabetes with ketoacidosis, type I (juvenile type), not stated as uncontrolled</td>
</tr>
<tr>
<td>250.13</td>
<td>Diabetes with ketoacidosis, type I (juvenile type), uncontrolled</td>
</tr>
<tr>
<td>250.21</td>
<td>Diabetes with hypertension, type I (juvenile type), not stated as uncontrolled</td>
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<td>250.23</td>
<td>Diabetes with hypertension, type I (juvenile type), uncontrolled</td>
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<td>250.31</td>
<td>Diabetes with other coma, type I (juvenile type), not stated as uncontrolled</td>
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<td>250.33</td>
<td>Diabetes with other coma, type I (juvenile type), uncontrolled</td>
</tr>
<tr>
<td>250.41</td>
<td>Diabetes with renal manifestations, type I (juvenile type), not stated as uncontrolled</td>
</tr>
</tbody>
</table>
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
E10.3523  Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
E10.3531  Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
E10.3532  Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye
E10.3533  Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
E10.3541  Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
E10.3542  Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
E10.3543  Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral
E10.3551  Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye
E10.3552  Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye
E10.3553  Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral
E10.3591  Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye
E10.3592  Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye
E10.3593  Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral
E10.36    Type 1 diabetes mellitus with diabetic cataract
E10.37X1  Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye
E10.37X2  Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye
E10.37X3  Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral
E10.39    Type 1 diabetes mellitus with other diabetic ophthalmic complication
E10.40    Type 1 diabetes mellitus with diabetic neuropathy, unspecified
E10.41    Type 1 diabetes mellitus with diabetic mononeuropathy
E10.42    Type 1 diabetes mellitus with diabetic polyneuropathy
E10.43    Type 1 diabetes mellitus with diabetic autonomic (poly)neuropathy
E10.44    Type 1 diabetes mellitus with diabetic amyotrophy
E10.49    Type 1 diabetes mellitus with other diabetic neurological complication
E10.51    Type 1 diabetes mellitus with diabetic peripheral angiopathy without gangrene
E10.52    Type 1 diabetes mellitus with diabetic peripheral angiopathy with gangrene
E10.59    Type 1 diabetes mellitus with other circulatory complications
E10.610   Type 1 diabetes mellitus with diabetic neuropathic arthropathy
E10.618   Type 1 diabetes mellitus with other diabetic arthropathy
E10.620   Type 1 diabetes mellitus with diabetic dermatitis
E10.621   Type 1 diabetes mellitus with foot ulcer
E10.622   Type 1 diabetes mellitus with other skin ulcer
E10.628   Type 1 diabetes mellitus with other skin complications
E10.630   Type 1 diabetes mellitus with periodontal disease
E10.638   Type 1 diabetes mellitus with other oral complications
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>Date</td>
<td>Changes</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>04-21-2005</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>11-02-2006</td>
<td>Added the definition of “intensive insulin therapy”.</td>
</tr>
<tr>
<td>01-02-2007</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></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></td>
<td>In “Description” section, deleted “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>
<tr>
<td></td>
<td>In “Documentation” section, deleted “Program Involvement (all required):” as recommended by the Medical Director.</td>
</tr>
<tr>
<td></td>
<td>In “Documentation” section, deleted #2 “Basal insulin usually involves “Ultralente” and “Lantus” insulin.” as recommended by the Medical Director.</td>
</tr>
<tr>
<td></td>
<td>In “Documentation” section, deleted #3 “Bolus insulin (insulin analogue) usually involves “Humalog” or “Novolog” insulin.” as recommended by the Medical Director.</td>
</tr>
<tr>
<td></td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>In “Reference” Government Agency; Medical Society; and Other Authoritative Publications section, added new #3 through #7.</td>
</tr>
<tr>
<td>Date</td>
<td>Action Description</td>
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<tr>
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</tr>
</tbody>
</table>
| 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 |
| 03-25-2011 | In Policy Guidelines section:
  - Added "or multiple daily injections" to read "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."
Updated Reference section. |
| 10-04-2013 | Updated Description section.
In Policy section:
  - Formatted medical policy language.
  - In Item C, #1, removed "symptomatic" to read "Patients with type I diabetes who have recurrent, unexplained, severe (generally blood glucose levels less than 50 mg/dl) hypoglycemia..."
  - In Item D, inserted "experimental/" to read "Other uses of continuous monitoring of glucose levels in interstitial fluid as a technique of diabetic monitoring are considered
<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>03-06-2015</td>
<td>Updated Description section.</td>
</tr>
<tr>
<td></td>
<td>In Coding section:</td>
</tr>
<tr>
<td></td>
<td>- Added ICD-10 Diagnosis <strong>(Effective October 1, 2014)</strong></td>
</tr>
<tr>
<td></td>
<td>Updated Reference section.</td>
</tr>
<tr>
<td>08-04-2016</td>
<td>Updated Description section.</td>
</tr>
<tr>
<td></td>
<td>In Policy section:</td>
</tr>
</tbody>
</table>
|            | - Removed Item E, "Use of artificial pancreas system, including but not limited to closed-loop monitoring devices with low-glucose suspend (LGS) features, are considered experimental / investigational."
|            | - In Policy Guidelines, add the following statements:
|            | o "Several insulin pump systems (eg, Omnipoq 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 inslin 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."
|            | o "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."
|            | In Coding section:                 |
|            | - Added ICD-10 Diagnosis **(Effective October 1, 2014)** |
|            | Updated Reference section.         |
|            | In Policy section:                 |
|            | - Removed Item E, "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."
|            | - In Policy Guidelines Item 1, removed "Omnipoq Insulin Management System," to read "Several insulin pump systems (eg, 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."
|            | Updated Rationale section.         |
|            | Updated References section.        |

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Contains Public Information
In Coding section:

In Policy section:
- In Policy Guidelines Item 3, removed "Women" and added "Individuals" to read, "Individuals with type I diabetes mellitus who are pregnant or about to become pregnant with poorly controlled diabetes are another subset of patients to which the policy statement on intermittent monitoring may apply."

In Coding section:
- Added CPT codes: 0446T, 0447T, 0448T.

In Coding section:
- Added HCPCS codes: K0553, K0554 (Effective July 1, 2017).

Updated Description section.

In Policy section:
- In Item A, removed "mellitus" to read, "Intermittent monitoring, ie, up to 72 hours, of glucose levels in interstitial fluid may be considered medically necessary in patients with type 1 diabetes whose diabetes is poorly controlled, despite current use of best practices (see Policy Guidelines). Poorly controlled type 1 diabetes includes the following clinical situations;"
- In Item C 1, added "or impaired awareness of hypoglycemia that" and removed "for whom hypoglycemia" to read, "Patients with type 1 diabetes 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;"
- Added new Item C 3, "Patients with poorly controlled type 1 diabetes who are present. Poorly controlled type 1 diabetes includes unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis;"
- Updated Policy Guidelines.

Updated Rationale section.

Updated References section.

REFERENCES


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.