Subject: Continuous Glucose Monitoring of the Interstitial fluid		Original Effective Date: 11/20/08
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PREFACE

This Medical Guidance is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the following website: http://www.cms.hhs.gov/center/coverage.asp.

FDA INDICATIONS

The FDA has approved the following continuous glucose monitoring systems (CGMS) that include but are not limited to: GlucoWatch® G2 Biographer (Animas Corp.); DexCom Seven™ Plus (DexCom Inc.), MiniMed CGMS, MiniMed Guardian® Real-Time System, MiniMed Paradigm® Real-Time System, and *i*Pro Continuous Glucose Monitor (Medtronic MiniMed Inc.); and the FreeStyle® Navigator Continuous Glucose Monitoring System (Abbott Diabetes Care).

CGMS are indicated for continually recording interstitial fluid glucose levels in people (ages 18 and older) with diabetes mellitus for the purpose of improving diabetes management. The FDA has clearly indicated that these devices are not to be used as a replacement for conventional fingerstick monitoring and glucose adjustment decision making. They are to be used in conjunction with conventional methods for tracking and trending data and long term decision making to determine when conventional testing would best be performed.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina medical coverage guidance (MCG) document and provide the directive for all Medicare members. The directives from this MCG document may be followed if there are no available NCD or LCD documents available and outlined below.

CMS currently does not have a national coverage determination (NCD) regarding general continuous glucose monitoring. CMS does have a NCD for the use of closed loop blood glucose control devices (e.g., Paradigm Real Time System). It is indicated for short term-management hospital bedside use for insulin dependent diabetic patients only in times of crisis. Potential crisis includes trauma, surgery, stress, labor and delivery, or

wide fluctuations in blood glucose levels. Its use is generally limited to a 24- to 48-hour period because of potential complications; (e.g., sepsis, thromboses, and nonportability, etc.). [8]

CMS does have local coverage determinations (LCD's) for intermittent continuous glucose monitoring systems (CGMS) and these devices are considered medically necessary in patients who have wide glycemic swings, frequent hospitalizations and complications of their diabetes. Coverage is limited to intermittent CGMS once every 6 months to improve diabetic control. [65]

INITIAL COVERAGE CRITERIA

Molina Healthcare may consider continuous glucose monitoring system (CGMS) of interstitial fluid medically necessary for adult members who are 18 years of age and over with type 1 insulin dependent diabetes when **ALL** of the following criteria have been met:

- ❑ Board certified endocrinologist prescribing CGMS; and
- ❑ Completion of a comprehensive diabetic education program; and
- ❑ Frequency of glucose self-testing at least 4 times per day [67] during the previous month; and
- ❑ Compliance with a plan recommended by a board certified endocrinologist [62]; and
- ❑ Insulin injections are required 3 or more times per day [66 68]; and
- ❑ FDA approved Device; and
- ❑ Only used for intermittent short term use (up to 3 days or 72 hours of consecutive use); and
- ❑ Insulin dose is adjusted based on self-testing results, **and** meets **one or more** of the following: [55 58 59 66]
    - Unexplained large fluctuations in daily blood glucose values before meals (>150 mg/dl) OR
    - Early morning fasting hyperglycemia in type 1 diabetics known as the "dawn phenomenon" (a rise in blood sugar levels before breakfast) OR
    - Recurrent episodes of severe hypoglycemia (blood glucose < 50mg/dl) despite appropriate modifications in insulin regime

CONTINUATION OF THERAPY

CGMS may only be used for intermittent short term use (up to 3 days or 72 hours) of consecutive use. Coverage is limited to intermittent CGMS once every 6 months. **Long term** use of CGMS is not covered.

COVERAGE EXCLUSIONS

Molina Healthcare ***does not consider*** continuous glucose monitoring of interstitial fluid medically necessary for the following indications [53]:

- ❑ In adult patients with type 2 diabetes

- ❑ In children and adolescents with type 1 diabetes who have not achieved adequate glycemic control despite frequent self-monitoring of fingerstick blood glucose levels

- ❑ In pregnant women with gestational diabetes or type 1 or 2 diabetes.

Molina Healthcare ***does not consider*** the use of any combined continuous subcutaneous insulin infusion and blood glucose monitoring system such as the MiniMed Paradigm medically necessary for any indication due to insufficient evidence to support its use [60].

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL

Continuous glucose monitoring systems (CGMS) are implantable or noninvasive devices that measure glucose levels in interstitial fluid at frequent intervals over a period of several days.[1] A sensor transmits results to a small recording device that can be worn on clothing, placed in a purse or kept within a short distance of the person.[12] The sensor will display and record blood glucose levels at short intervals, allowing observation of these levels. An alarm display can be set to notify a patient of high or low glucose levels. The information can be obtained in real time or retrospectively to guide a physician in therapy adjustments, with an overall goal of improving glycemic control. The glucose values obtained from these devices are not intended to replace standard fingerstick self monitoring of blood glucose (SMBG) but are used as an adjunct technique to supply additional information on glucose trends that are not available from self monitoring.[1,12]

GlucoWatch® G2® Biographer (Cygnus, Inc.)[2]

Note: This product has not been available since July 31, 2008

The GlucoWatch Biographer is indicated for detecting trends and tracking patterns in glucose levels in children over age 7 and adults with diabetes. This device is worn on the wrist like a watch and takes noninvasive measurements through the skin every 10 minutes for up to 13 hours. It has a high and low alarm feature for detecting episodes of hypoglycemia and hyperglycemia. The device is intended for use an adjunctive device to supplement and not replace information contained from standard glucose monitoring devices. Interpretation of results are based upon trends and patterns seen with several readings over time.

MiniMed Continuous Glucose Monitoring System (Medtronic, Inc)[3]

The MiniMed system contains a small glucose sensor that is placed into the subcutaneous tissue in the abdomen. A glucose monitor worn on the belt like a pager is connected by a cable to the glucose sensor. Measurements of interstitial fluid glucose concentrations are taken every 10 seconds, in terms of electrical potential, and averaged over a 5 minute period. Data are reviewed retrospectively by a trained healthcare provider. MiniMed is intended for occasional use and to discover trends in glucose levels during the day. It does not provide individual test readings and cannot be used for typical day-to-day monitoring. Measurements are collected for up to a 72 hour period. Evaluating trends over time are taken to help the patient know the best time to perform standard fingerstick testing.

MiniMed Guardian RT (Medtronic, Inc.)[4]

The Guardian system is intended for continuous or periodic monitoring of glucose levels in fluid underneath the skin for children over age 7 and adults. The device alerts if a glucose level falls or rises above a preset level. Values are not intended to be used directly for making therapy adjustments but to provide an indication of when a finger stick may be required. Therapy adjustments should be based upon on a home glucose monitor and not on Guardian values. Glucose data can be downloaded for an analysis of historical glucose values.

MiniMed Paradigm (Medtronic, Inc.)[5]

The Paradigm system is designed to be used in conjunction with an external insulin pump and for periodic or continuous monitoring of interstitial glucose levels children over age 7 and adults. The system provides an alert if glucose levels fall outside of preset parameters. Glucose values obtained from the system are not intended to be used for therapy adjustments but to indicate when a fingerstick may be required.

DexCom STS CGM System (DexCom, Inc.)[6]

This device is indicated for detecting trends and tracking patterns in adults 18 years of age and older with diabetes. The device is inserted into subcutaneous tissue in the abdomen for continuous glucose monitoring. The system tracks real time information for up to 72 hours. It aids in the detection of hypoglycemia or hyperglycemia to facilitate long term therapy adjustment. It is intended for use as an adjunctive device to complement and not replace information obtained from SMBG devices.

DexCom STS-7 Continuous Glucose Monitoring System (DexCom, Inc.)[7]

This device is indicated for detecting trends and tracking patterns in adults 18 years of age and older with diabetes. The device is inserted into subcutaneous tissue in the abdomen for continuous glucose monitoring. The STSD-7 measures glucose levels every five minutes throughout a seven day period. It is designed to assist in detecting hypoglycemia or hyperglycemia during overnight hours, between meals and provide input on how exercise and diet may affect glucose levels. It is intended for use as an adjunctive device to complement and not replace information obtained from SMBG devices.

Freestyle Navigator (Abbott Laboratories, Inc)

This device is indicated for adults 18 years of age and older with diabetes. The sensor for this device is placed on the back of the upper arm or on the abdomen. The device has warning alarms to detect hypoglycemic or hyperglycemic episodes. Glucose readings can be taken every minute for real-time access. The technology projects glucose direction and rate of change. It is not intended to replace traditional blood glucose monitoring devices and traditional methods must be performed before adjusting therapy for diabetes management.

*i*Pro Continuous Glucose Monitor (Medtronic MiniMed Inc.) [63]

This is a prescription-use only device that provides a 3-day evaluation of glucose levels. The device has a subcutaneous sensor that records glucose levels every 5 minutes for 3 days, and is designed for occasional use, rather than everyday use. The *i*Pro System is intended to continuously record interstitial glucose levels in diabetic individuals, but the readings are not available directly to patients in real time, and the readings are available for review by physicians after the entire 72-hour recording interval. Available data are designed to

identify patterns of glucose level excursions above or below the desired range, facilitating therapy regimen adjustments that may minimize these excursions.

GENERAL INFORMATION

Summary of Medical Evidence

Continuous Glucose Monitoring System Reliability

A study was conducted using the MiniMed CGMS to measure the accuracy of interstitial levels compared with plasma glucose levels. Interstitial glucose concentrations measured by the glucose sensor resulted in lower glucose values compared with venous plasma glucose when acute increases in blood glucose concentrations occurred.[16] A study of 11 adults (2 normal nondiabetic patients, 3 Type 2 diabetics, and 6 Type I diabetics) wore two interstitial CGMS simultaneously reproduced results that question the reliability of the sensors. Approximately 7 percent of the measurements varied by over 50 percent, and over 70 percent of the measurements varied by 10 percent or more.[19]

According to McCullough et al (2008). "The CGMS tend to be less accurate in the lower glucose range (<70mg/dL or 3.9 mmol/L) and may be inadequate for reliably detecting hypoglycemia. In one study, 91 children and adolescents wore one or two CGMS; the absolute median difference between over 400 paired hypoglycemic blood glucose values was 19mg/dL (1.0) mmol/L), with 42 percent of values falling within 15 mg/dl (0.9mmol/L) of the reference glucose."[21] The FDA labeling for various CGMS requires that these sensing devices are used in conjunction with daily fingerstick testing and should not be used exclusively for managing treatment changes for a patient. Other studies reporting preliminary data indicate a 96 to 98 percent of glucose sensor results from implantable CGMS in Type 1 diabetic patients fell within an acceptable margin of error when evaluating between a 5 to 90 day timeframe.[22,23]

The Diabetes Research in Children Network Study group evaluated the accuracy of several CGMS. The FreeStyle Navigator CGMS in children with Type 1 diabetes was compared with reference serum glucose values. The study results concluded ""the Navigator's accuracy does not yet approach the accuracy of current generation home glucose meters but is sufficient to believe that the device has the potential to be an important adjunct to treatment of youth with type 1 diabetes."[31] The Glucowatch G2 biographer (GW2B) and CGMS accuracy during hypoglycemia was evaluated. The conclusion indicated "the GW2B and the CGMS do not reliably detect hypoglycemia. Both of these devices perform better at higher glucose levels, suggesting they may be more useful in reducing HbA1C levels than in detecting hypoglycemia."[18]

The effectiveness of CBGM on controlling glycemic levels has not been studied widely, and in the studies conducted, has shown variable outcomes. A randomized-control study of 156 adults and children with poorly controlled type 1 diabetes were randomly assigned to self-monitoring blood glucose (SMBG) five times a day for 3 months, CGMS intermittently or CGMS continuously. [15] Initial data suggest that real-time CGMS gradually improved glycemic control resulting in an A1C reduction by 1% in 50 percent of the patients and by 2% in one quarter.[15] One study indicated that "the patients did not register specific information about their self management of diabetes therapy on a daily basis. Therefore, we cannot delineate in detail the link between the use of real-time CGM and the improvement in glycemic control."[15] A significant A1C reduction of 1% was

noted in the continuous CGMS group compared with the other two groups. The intermittent CGMS group did not show a statistically significant reduction in A1C.[15]

A second randomized-control trial of Type I (n= 75) and Type II diabetics (n=16) using CGMS showed less hypoglycemic and hyperglycemic events, remained within the target glucose range for longer time periods, and patients experienced less nocturnal hypoglycemia, although A1C levels had no statistically significant difference among the groups.(CGMS or SBMG)[13] A third study compared 128 poorly controlled insulin patients receiving either CGMS or SMBG (four or greater times daily).[14] The CGMS group experienced less hypoglycemic events at the 12 week follow-up. Improvements in A1C levels were the same at the12 week follow-up.

A retrospective review of 46 Type 1, insulin-dependent diabetic patients ranging in age from 12.8 years to 25.9 years evaluated the effectiveness of a 72 hour CGMS in identifying undetected hypoglycemia (e.g., <70) and postprandial hyperglycemia (e.g., 140mg/dL two hours after lunch). No statistically significant differences were identified in mean capillary glucose compared with CGMS (p=0.79). CGMS demonstrated a significantly more efficient detection in glycemic excursion (p=0.001). CGMS identified 58.2% of patients with unrecognized hypoglycemic events and 76.9% of patients with postprandial hyperglycemia episodes. CGMS versus blood glucose hyperglycemia was significant (p=0.002) and normoglycemia (p=0.05). Hypoglycemic values were not significantly different between CGMS and conventional blood glucose monitoring (p=0.16). Study limitations included a small heterogeneous population, a retrospective design with short term follow-up.

Adult Patients using CBGS

A large randomized controlled trial did not demonstrate a statistically significant decrease in glycosolated hemoglobin levels in adult diabetics using CGMS.[34] A second randomized controlled study revealed that both CGMS and SBGM had significant reductions in glycoslated hemoglobin compared with baseline levels up to 12 weeks, there were no significant differences experienced between the two groups.[37] Patients monitored by CGMS experienced a significantly reduced duration of hypoglycemia after 12 weeks then the SBGM monitored group.[37] A small prospective controlled trial noted that 41% of hypoglycemic events were not recognized by the CGMS. The CGMS also appeared to over report hypoglycemic events.[35] The effectiveness of alarms from real-time sensor glucose values were evaluated.[36] A significantly reduced duration of hypoglycemic events were noted when compared with controls as a result of patient responses from the hypoglycemia alerts. A small increase in hyperglycemic events compared with the control group was also reported but may have resulted from overtreatment of hypoglycemia.[36] A significantly greater number of hypoglycemia and postprandial hyperglycemia events were detected with CGMS than with SBGM. A high number of sensors (28%) required replacement after insertion due to malfunction.[38] A 12 week observational study of A1c levels in both Types 1 and 2 diabetics being treated with oral agents or insulin. CGM was used as an adjunct to fingersticks for treatment decision making. A1c was reduced by 0.4 $\pm$ 0.05% (p<0.0001). The study limitation was a lack of control group making it difficult to attribute a causal link between CGMS use and the HbA1c reduction.[49]

The Minimally Invasive Technology Role and Evaluation (MITRE) randomized controlled trial was conducted to evaluate whether the additional information provided by minimally invasive glucose monitors results in improved glycaemic control in people with poorly controlled insulin-requiring diabetes, and to assess the acceptability and health economic impact of the devices. 404 people aged over 18 years with insulin-treated

diabetes mellitus (types 1 or 2) for at least 6 months who were receiving two or more injections of insulin daily were evaluated. Participants had to have had two glycosylated hemoglobin (HbA1c) values > or = 7.5% in the last 15 months. Two groups received minimally invasive continuous glucose monitoring devices [GlucoWatch Biographer or MiniMed and the other two groups received standard clinical management for diabetes. At 18 months all groups demonstrated a decline in HbA1c levels from baseline. 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 standard treatment. The authors concluded that continuous glucose monitors do not lead to improved clinical outcomes and are not cost-effective for improving HbA1c in unselected individuals with poorly controlled insulin-requiring diabetes. [56]

Children Using CGMS

Two studies reported a reduction in glycosolated hemoglobin levels using CGMS,[41,44] one study did not show a statistically significant decrease in these levels.[40] Two of these studies indicated that a CGMS showed a statistically significant increase in the identification of hypoglycemic events, the impact of detecting these events on health outcomes or patient management were not supported by clinical data.[40,44] A 12-week controlled trial of 36 children diagnosed with diabetes showed no difference in glycemic control by evaluating A1C levels in children using continuous versus intermittent glucose monitoring.[10] An uncontrolled study of 19 children less than 7 years of age with Type 1 diabetes was conducted to detect and improve glycemic patterns using CGMS; significant changes were not detected.[30] The DirectNet group evaluated the GlucoWatch biographer compared with SMBG and did not report statistically significant glycosolated hemoglobin or frequency of hypoglycemic levels in pediatric patients.[39,42] A small randomized trial reported a small decrease in glycosolated hemoglobin levels after 6 months compared with the control group.[43] Levitsky et al. (2008) indicate "the value of continuous monitoring appears to lie more in detecting patterns of blood glucose fluctuations and episodes of hypoglycemia during periods of sleep. However, the currently available continuous monitoring systems are relatively inaccurate in the lower (<70mg/dL) glucose range, limiting their usefulness."[11] Continuous blood glucose monitoring is not provided as a recommendation in management in children and adolescents.[11]

Pregnant women with CGMS

Two studies evaluated the use of CGMS in pregnant women. One study reviewed gestational diabetes and reported an increased detection of longer and more frequent periods of hyperglycemia. CGMS was able to differentiate patients with impaired glucose tolerance, patients with gestational diabetes, from nondiabetic pregnant women.[45] A second study reported a reduction in nocturnal hypoglycemic and undetected hyperglycemic events when CGMS was used to adjust insulin treatment. The study did not report a difference in perinatal or clinical outcomes from use of either CGMS and SMBG.[46]

A recent study compared CGMS with SMBG needing. Pregnant women at 22–34 gestational weeks had at least two abnormal high values out of three in OGTT.[47] Patients were randomly allocated to have CGMS (*n*=36) or SMG (*n*=37). Dietary counseling was similar in both groups. Patients tested their plasma glucose 5 times per day. Need of antidiabetic treatment was determined using the following cut-off values: fasting plasma glucose >5.5mmol/L twice or > 5.5mmol/l once and postprandial value >7.8mmol/l, or postprandial value at least twice

above 7.8mmol/l. In 11 out of 36 patients (31%) monitored with CGMS® antihyperglycemic drug treatment was introduced (difference between groups, *p*=0.0149). There were no statistically significant differences between the groups regarding maternal age, pre-pregnancy BMI, HbA1c, gestational weeks at delivery, rate of pregnancy-induced hypertension, rate of caesarean section, infant birth weight or neonatal hypoglycaemia.

The authors concluded that **"**Continuous glucose monitoring system detects a markedly higher proportion of GDM mothers needing antihyperglycemic medication compared with self-monitoring of plasma glucose. Further large-scale studies are needed to evaluate whether CGMS® guided initiation of antihyperglycemic therapy results in less macrosomia and perinatal complications related to GDM."[47]

Complications Associated with the Use of CGMS

Continuous glucose monitoring is generally considered a safe device.[1] The most commonly reported adverse events include redness, itching, irritation, discomfort, burning, hypersensitivity and bleeding at the sensor insertion or contact site.[1,32] Inappropriate insulin dosing is unlikely to occur as self monitoring of blood glucose levels is required and recommended while using CGMS.[1]

Technology Assessments/Systematic Reviews/Meta-analysis

A systematic review and meta-analysis was conducted to determine if CGMS leads to improved HBA1c levels. A total of seven randomized control trials consisting of 335 patients met the inclusion criteria. The duration of the studies ranged from 12 to 24 weeks. Five studies focused on the pediatric population age 18 or younger. CGMS compared with self blood glucose monitoring (SBGM) by fingerstick method was associated with a nonsignificant reduction in HBA1c levels (95% CI, p=0.055). The authors concluded "there is insufficient evidence to support the notion that CGMS provides a superior benefit over SBGM in terms of HBA1c reduction. There was some indication of improved detection of asymptomatic nocturnal hypoglycemia in the CGMS group."[26] An analysis of the pediatric population separately observed a significant reduction in HBA1c in favor of CGMS (95% CI: -0.71% to -0.02%, p=0.036).[26]

A second systematic review and meta-analysis was conducted to review the effects of CGMS with SBGM in children with Type I diabetes.[27] Five randomized-control trials consisting of 131 Type I diabetic patients were combined in the evaluation. The combined data did not show a statistically significant reduction in HBA1c levels. The CGMS showed a significant number of insulin dose changes needed per month when compared with the control groups. (mean difference 6.3 changes, 95% CI 2.88-9.72). The authors concluded "the continuous glucose monitoring system is not better than self-monitoring of blood glucose with regard to improvement of metabolic control among type I diabetic children. However, due to the small number of participants and methodological limitations of the studies included, findings of this meta-analysis should be interpreted with caution."[27]

A third systematic review and meta analysis was conducted to assess the efficacy and safety of various CGM systems compared with self blood glucose monitoring (SMBG). 14 randomized controlled trials consisting of 1268 type 1 diabetics were analyzed. The combined data showed that patients using CGM had a greater decrease in hemoglobin A1c (HbA1c) from baseline compared with those using SMBG (WMD -0.26% [-0.34; -

0.19]). Only real-time devices for CGM improved glycemic control (WMD -0.27% [-0.34; -0.19]). The authors concluded CGM, particularly its real-time system, has a favorable effect on glycemic control and decreases the incidence of hypoglycemic episodes in both adult and pediatric patients with type 1 diabetes.

Another systematic review was conducted recently to review the effect of real-time continuous glucose monitoring systems in diabetes management. Nine randomized controlled trials were identified with a focus on the seven studies because the other two used a device not on the market currently. Six of seven studies showed some positive effect of real-time continuous glucose monitoring systems on HbA(1c) (HbA(1c) decrease 0.3-0.7% or 3-8 mmol/mol). In some studies, this effect only was shown in subgroups (compliant adult patients). However, the size of effect may be underestimated by better-than-average results in the control group, as self-monitoring blood glucose measurements are carried out more frequently than in usual clinical practice. Despite the goal of lowering HbA(1c) , no more severe hypoglycemic episodes were seen, except in one study. In contrast, no positive effect was shown with the real-time continuous glucose monitoring system on hypoglycaemia, but randomized controlled trials were not designed or powered to investigate this issue. Time in different glucose strata was assessed only in some trials: two of them showed a significant but small increase in time in euglycaemia. The authors concluded that current evidence shows that the real-time continuous glucose monitoring system has a beneficial effect on glycaemic control in adult diabetes patients, without an increase in the incidence of hypoglycaemia. Studies in well-selected patient groups (pregnancy, history of severe hypoglycemias, Type 2 diabetes) are lacking. [54]

A technology assessment was conducted by the New Zealand Health Technology Group, 2006.[28] The following advisory committee summary and recommendation was given, "Evidence from RCT's, though somewhat contradictory and limited by small and select patient groups, indicates some effectiveness in glycemic control and increased safety due to greater awareness of glycemic variation but these devices are less accurate, particularly during hypoglycemic episodes and can cause minor skin reactions, and do not improve diabetes related quality of life, compared with SMBG. CGMS is useful as an adjunct to conventional (standard blood glucose self-monitoring) SMBG in selected patients with difficulties maintaining glycemic control. However, at this stage, CGMS will not replace conventional SMBG in the majority of patients."[28]

A critical appraisal was conducted in response to evidence review.[48] The author indicated that studies evaluating real-time CGM systems have demonstrated an improvement in the time an individual experiences a normal glucose range. Only one of these studies had a decrease in HbA1c.[41] These findings should be considered with caution. The author states "the low values of interstitial glucose may not represent true hypoglycemia…the clinical significance of these findings remains to be established. A clear demonstration is needed that the decreased time spent in hypoglycemia has a clinical impact on the unawareness syndrome, the rate of severe hypoglycemia, or the number of hospital days. On the other hand, it appears that in some patients, use of the system will increase the risk of severe hypoglycemia, as a consequence of insulin over bolusing in response to the display of a high glucose concentration."[48] One other study showed convincing results that CGMS can improve HbA1c.[15] The author identifies the main advantage of CGMS being the alarm feature available, although these systems do not reliably detect hypoglycemia. Data from real-time systems did not report the specificity or sensitivity results for review.

CGMS are recommended by one evidence based resource "only for patients with type 1 diabetes who use intensive insulin therapy, often with an insulin pump"[12]. The drawbacks for use of the pump are recorded as not being as accurate as blood glucose monitors. CGMS has shown to be less accurate with rapidly rising and lower range glucose levels (70mg/dL) and "may be inadequate for reliably detecting hypoglycemia."[12]

Hayes, Cochrane, UpToDate, MD Consult etc.

Hayes Directory for Continuous Glucose Monitoring Systems[1]

CGMS is supported by some positive published data regarding safety and/or efficacy for adult, adolescent, and pediatric patients with type I diabetes who have not achieved adequate glycemic control with fingerstick self monitoring of glucose levels. A beneficial impact on health outcomes has not been proven as data are inconsistent or conflicting. Some of the studies reviewed reported significantly reduced incidences of hypoglycemia and hyperglycemia and improved glycemic control. Other studies reported no improvement in outcomes including glycosylated hemoglobin (HbA_{1c}). Data also suggests there is no proven benefit in improving glycemic control for patients with type 2 diabetes and women with gestational diabetes. All studies were not considered high quality as several were methodologically flawed, had lack of blinding, lack of follow-up and small sample populations. There was lack of standardization in the duration of CGMS and varied definitions of what was considered hypoglycemic and hyperglycemic events.

In a recent Hayes Directory Report for Continuous Glucose Monitoring Systems [53] there is evidence from a number of randomized controlled trials that the use of continuous glucose monitoring systems may contribute to improved glycemic control and decreased glycosylated hemoglobin levels in adult patients with type 1 diabetes. A few studies did not report a significant difference between CGM and self-monitoring of blood glucose (SMBG). Similar results were found for adult patients with type 2 diabetes, although the evidence was more limited. In pediatric patients with type 2 diabetes results of studies of CGM devices were mixed; some studies reported significantly improved glycemic control and reduced incidences of hyperglycemia and hypoglycemia, while other studies reported no improvement in these or other outcome measures, such as glycosylated hemoglobin (HbA_{1c}) levels. Studies evaluating the use of CGM devices to detect hyperglycemia and perinatal outcomes are limited in n pregnant women with either type 1 or gestational diabetes. There was not enough available evidence to draw conclusions regarding the efficacy of CGM devices in pregnant women with type 2 diabetes.

A Hayes Brief for MiniMed Paradigm[9]

Data suggests there is no proven benefit based upon lack of sufficient data to provide conclusive evidence that this system is effective and safe. Outcomes reported in studies were associated with better glucose level maintenance but data did not report if this was a statistically significant outcome. Small populations were evaluated for short timeframes; controlled studies with long term data were lacking

A Hayes Brief for the MiniMed Paradigm® REAL-Time System [60]

Data fails to provide conclusive evidence that closed-loop use of the Paradigm REAL-Time System is a safe and effective method for blood glucose management. Only one of the studies reported that closed-loop insulin management was associated with better maintenance of glucose levels in the targeted range. Additionally, this system has only been tested in closed-loop mode for short periods of time in a small number of patients who were receiving high levels of medical care. Therefore, it is unclear whether this treatment will provide long-term benefits for patients under normal conditions. In order to assess the safety and efficacy of the Paradigm System in closed-loop mode. Controlled studies with larger numbers of patients and longer periods of closed-loop insulin management are needed.

Cochrane [64]

A Cochrane review was conducted through June 2, 2011 to evaluate the effects of CGMS compared to conventional self-monitoring of blood glucose (SMBG) in patients with type 1 diabetes mellitus. The results of the meta-analyses of 22 randomized controlled studies indicated benefit of CGM for patients starting on CGM sensor augmented insulin pump therapy compared to patients using multiple daily injections of insulin and standard monitoring blood glucose. There was a significant larger decline in HbA1c level for real-time CGM users starting insulin pump therapy compared to patients using multiple daily injections and standard monitoring blood glucose after 6 months time. For those patients starting with CGM only, the average decline in HbA1c level six months after baseline was also statistically significantly larger for CGM users compared to SMBG users, but much smaller than for patients starting using an insulin pump and CGM at the same time. On average, there was no significant difference in risk of severe hypoglycaemia or ketoacidosis between CGM and SMBG users. Health-related quality of life was reported in five of the 22 studies. None of these studies showed a significant difference between CGM and SMBG. There were no studies in pregnant women with diabetes type 1 and in patients with hypoglycaemia unawareness. The authors concluded that there is limited evidence for the effectiveness of real-time continuous glucose monitoring (CGM) use in children, adults and patients with poorly controlled diabetes. The largest improvements in glycaemic control were seen for sensor-augmented insulin pump therapy in patients with poorly controlled diabetes who had not used an insulin pump before. The risk of severe hypoglycaemia or ketoacidosis was not significantly increased for CGM users.

UpToDate [61]

Data suggests that real time continuous glucose monitoring systems have the potential to improve glycemic control while decreasing the number of hypoglycemic episodes but the efficacy remains uncertain when compared to self monitoring of blood glucose. CGMS may also be helpful in controlling daily fluctuations in blood glucose.

Professional Organizations

The American Diabetes Association Position Statement (2004) states, “continuous ambulatory blood glucose testing may be used to determine 24-hour blood glucose patterns and to detect unrecognized hypoglycemia, however, its role in improving diabetes outcomes remains to be established”[25]

The American Diabetes standards of medical care (2008) indicate, “The introduction of real-time blood glucose

monitoring as a tool for outpatient diabetes management has potential benefit for the inpatient population. However, at this time, data are lacking examining this new technology in the acutely ill patient population. Until more studies are published, it is premature to use continuous blood glucose monitoring in the hospital except in a research setting."[24] Continuous glucose monitoring may be a supplemental tool to SMBG for selected patients with type 1 diabetes, especially those with hypoglycemia unawareness."[24] This recommendation is based upon a rating designated as expert consensus or clinical experience and not published medical evidence. The American Diabetes standards of medical care (2011) indicate that continuous glucose monitoring (CGM) in conjunction with intensive insulin regimens can be a useful tool to lower A1C in selected adults (age ≥25 years) with type 1 diabetes. [51]

The American Association of Clinical Endocrinologists medical guidelines recommend to "arrange for continuous glucose monitoring for patients with T1DM with unstable glucose control and for patients unable to achieve an acceptable HbA1c level; continuous glucose monitoring is particularly valuable in detecting both unrecognized nocturnal hypoglycemia and postprandial hyperglycemia."[50] The guidelines were updated in 2010 and currently the American Association of Clinical Endocrinologists (AACE) recommends personal CGM for the following patients [58]:

- Those with type 1 DM and the following characteristics:
  - Hypoglycemic unawareness or frequent hypoglycemia judged to be excessive, potentially disabling, or life-threatening
  - Excess glycemic variability
  - Requiring HbA1c reduction without increased hypoglycemia
  - During preconception and pregnancy
- Children and adolescents with type 1 DM who have achieved HbA1c levels less than 7.0% (these patients and their families are typically highly motivated)
- Youth with type 1 DM who have HbA1c levels of 7.0% or higher and are able to use the device on a near- daily basis

The National Institute for Health and Clinical Excellence (NICE) published guidelines in 2004 for children and young adults with Type 1 diabetes. The guideline recommendations indicate "Children and young people with type 1 diabetes that have persistent problems with hypoglycaemia unawareness or repeated hypoglycemia or hyperglycemia should be offered continuous glucose monitoring systems."[33] These guidelines were modified in 2011 and indicate that adults with repeated hyper or hypoglycemic episodes in the same day or hypoglycemic unawareness unresponsive to insulin dose adjustment be offered continuous glucose monitoring systems. [59]

The Endocrine Society recently published clinical practice guidelines for continuous glucose monitoring. These guidelines recommend that the approved devices may be used in children and adolescents with type 1 diabetes mellitus to assist in maintaining target hemoglobin A1c (HbA1c) levels while limiting the risk of hypoglycemia. This recommendation is based on weaker evidence. The use of CGM devices by adult patients is recommended for those who have demonstrated that they can use these devices on a nearly daily basis. CGM should not be used 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. [62]

CODING INFORMATION

CPT	Description
95250	Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for up to 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 up to 72 hours; physician interpretation and report
99091	Collection and interpretation of physiologic data (e.g., ECG, blood pressure, glucose monitoring) digitally stored and/or transmitted by the patient and/or caregiver to the physician or other qualified health care professional, requiring a minimum of 30 minutes of time

HCPCS	Description
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
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	Description
250-250.93	Diabetes Mellitus

ICD-10	Description
E11.9	Type 2 diabetes mellitus without comp
E13.9	Oth spec diabetes mellitus w/o comp
E10.9	Type 1 diabetes mellitus w/o comp
E11.65	Type 2 diabetes mellitus w hyperglycemia
E10.65	Type 1 diabetes mellitus w hyperglycemia
E11.69	Type 2 diabetes mellitus w other spec complication
E13.10	Other spec diab w/ketoacidosis w/o coma
E10.10	Type 1 diabetes mellitus w/ketoacidosis w/o coma

E11.65 & E11.69	Type 2 diabetes mellitus w/oth spec comp
E11.69	Type 2 diabetes mellitus w/hyperglycemia
E10.10 & E10.65	Type 1 diabetes mellitus w/ketoacidosis w/o coma
E10.65	Type 1 diabetes mellitus w/hyperglycemia
E11.00	Type 2 DM w/hyperosmolarity w/o nkhhc
E11.01	Type 2 DM w/hyperosmolarity w coma
E13.00	Oth spec DM w/hyperosmolarity w/o nkhhc
E13.01	Oth spec DM hyperosmolarity coma
E10.69	Type 1 DM w/oth spec complication
E11.00 & E11.65	Type 2 DM w/hyperosmolarity w/o nkhhc
E11.65	Type 2 DM with hyperglycemia
E10.65	Type 1 diabetes mellitus w/hyperglycemia
E10.69 & E10.65	Type 1 DM w/oth spec complication
E11.641	Type 2 DM w/hypoglycemia w/coma
E13.11	Oth spec DM w/ketoacidosis w/coma
E13.641	Oth spec DM w/hypoglycemia w/coma
E10.11	Type1 DM w/ketoacidosis w/coma
E10.641	Type 1 DM w/hypoglycemia w/coma
E11.01 & E11.65	Type 2 DM w/hyperosmolarity w/coma
E11.65	Type 2 DM w/hyperglycemia
E10.11 & E10.65	Type 1 DM w/ketoacidosis w/coma

E10.65	Type 1 DM w/hyperglycemia
E11.21	Type 2 DM w/diabetic nephropathy
E11.22	Type 2 DM w/diab chronic kidney dx
E11.29	Type 2 DM w/oth diab kidney comp
E13.21	Oth spec DM w/diab nephropathy
E13.22	Oth spec DM diab chron kidney dz
E13.29	Oth spec DM w/oth diab kidney comp
E10.21	Type 1 DM w/diabetic nephropathy
E10.22	Type 1 DM w/diab chron kidney dz
E10.29	Type 1 DM w/oth diab kidney comp
E11.21 & E11.65	Type 2 DM w/diabetic nephropathy
E11.65	Type 2 DM w/hyperglycemia
E10.21 & E10.65	Type 1 DM w/diabetic nephropathy
E10.65	Type 1 DM w/hyperglycemia
E11.311	Type 2 DM w/uns diab retinopathy w/macular edema
E11.319	Type 2 DM w/uns diab retinpath w/o macular edema
E11.321	Type 2 DM w/mild nonprolif diab retinopathy w/me
E11.329	Type 2 DM w/mild nonprolif diab retinpath w/o me
E11.331	Type 2 DM w/mod nonprolif diab retinopathy w/me
E11.339	Type 2 DM w/mod nonprolif DM retinopathy w/o me
E11.341	Type 2 DM w/sev nonprolif diab retinopathy w/me
E11.349	Type 2 DM w/sev nonprolif diab retinopathy w/o me
E11.351	Type 2 DM w/proliferative diab retinopathy w/me
E11.359	Type 2 DM prolif DM retinopathy no macular edema
E11.36	Type 2 DM wih diabetic cataract
E11.39	Type 2 DM other diab ophthalm comp

E13.311	Oth DM w/uns diab retinopathy w/macular edema
E13.319	Oth spec DM w/uns diab retinopathy w/o me
E13.321	Oth spec DM mild nonprolif diab retinopathy w/me
E13.329	Oth DM w/mild nonprolif diab retinopathy w/o me
E13.331	Oher spec DM mod nonprolif diab retinopathy w /me
E13.339	Oth spec DM mod nonprolif diab retinpath w/o me
E13.341	Oth spec DM sev nonprolif diab retinopathy w/me
E13.349	Oth DM w/sev nonprolif diab retinopathy w/o me
E13.351	Oth DM w/prolif diab retinopathy w/macular edema
E13.359	Oth DM w/prolif diab retinopath no macular edema
E13.36	Oth spec DM w/diabetic cataract
E13.39	Oth spec DM w/oth diab ophthalm comp
E10.311	Type 1 DM w/uns diab retinopathy w/macular edema
E10.319	Type 1 DM w/uns diab retinpath w/o macular edema
E10.321	Type 1 DM w/mild nonprolif diab retinopathy w/me
E10.329	Type 1 DM mild nonprolif diab retinpathy w/o me
E10.331	Type 1 DM w/mod nonprolif diab retinpathy w/me
E10.339	Type 1 DM w/mod nonprolif diab retinpathy w/o me
E10.341	Type 1 DM w/severe nonprolif diab retinpath w/me
E10.349	Type 1 DM w/sev nonprolif diab retinopath w/o me
E10.351	Type 1 DM w/prolif diabetic retinopathy w/me
E10.359	Type 1 DM w/prolif diab retinpath w/o me
E10.36	Type 1 DM w/diabetic cataract
E10.39	Type 1 DM w/oth diab ophthalmic comp
E11.311 & E11.65	Type 2 DM w/uns diab retinopathy w/macular edema
E11.319 & E11.65	Type 2 DM w/uns diab retinpath w/o macular edema

E11.36 & E11.65	Type 2 DM wih diabetic cataract
E11.39 & E11.65	Type 2 DM oth diab ophthalm comp
E11.65	Type 2 DM with hyperglycemia
E10.311 & E10.65	Type 1 DM w unsp diab retinopathy w macular edema
E10.319 & E10.65	Type 1 DM w/uns diab retinpath w/o macular edema
E10.36 & E10.65	Type 1 DM w diabetic cataract
E10.39 & E10.65	Type 1 DM w/oth diab ophthalmic comp
E10.65	Type 1 DM with hyperglycemia
E11.40	Type 2 DM w/diab neuropathy unspec
E11.41	Type 2 DM w/diab mononeuropathy
E11.42	Type 2 DM w/diab polyneuropathy
E11.43	Type 2 DM w/diab autonomic polyneuro
E11.44	Type 2 DM w/diab amyotrophy
E11.49	Type 2 DM w/oth diab neuro comp
E11.610	Type 2 DM w/diab neuropathic arthropathy
E13.40	Oth spec DM w/diab neuropathy unspec
E13.41	Oth spec DM w/diab mononeuropathy
E13.42	Oth spec DM w/diab polyneuropathy
E13.43	Oth spec DM w/diab autonomic polyneuropathy
E13.44	Oth spec DM w/diab amyotrophy
E13.49	Oth spec DM w/oth diab neurological comp

E13.610	Oth spec DM w/diab neuropathic arthropathy
E10.40	Type 1 DM w/diab neuropathy uns
E10.41	Type 1 DM w/diab mononeuropathy
E10.42	Type 1 DM w/diab polyneuropathy
E10.43	Type 1 DM w/diab autonomic polyneuropathy
E10.44	Type 1 DM w/diab amyotrophy
E10.49	Type 1 DM w/oth diab neurological comp
E10.610	Type 1 DM w/diab neuropathic arthropathy
E11.40 & E11.65	Type 2 DM w/diab neuropathy unspec
E11.65	Type 2 DM with hyperglycemia
E10.40 & E10.65	Type 1 DM w/diab neuropathy uns
E10.311 & E10.65	Type 1 DM w unsp diab retinopathy w macular edema
E10.65	Type 1 DM wih hyperglycemia
E11.51	Type 2 DM w/diab periph angiopathy w/o gangrene
E11.52	Type 2 DM w/diab periph angiopathy w/gangrene
E11.59	Type 2 DM w/oth circulatory comp
E13.51	Oth spec DM w/diab periph angiopathy no gangrene
E13.52	Oth spec DM w/diab periph angiopathy w/gangrene
E13.59	Oth spec DM oth circulatory comp
E10.51	Type 1 DM w/diab periph angiopathy w/o gangrene
E10.52	Type 1 DM w/diab periph angiopathy w/ gangrene
E10.59	Type 1 DM w/oth circulatory comp
E11.51 & E11.65	Type 2 DM w/diab periph angiopathy w/o gangrene

E11.65	Type 2 DM with hyperglycemia
E10.51 & E10.65	Type 1 DM w/diab periph angiopathy w/o gangrene
E10.65	Type 1 DM with hyperglycemia
E11.618	Type 2 DM w/oth diab arthropathy
E11.620	Type 2 DM w/diabetic dermatitis
E11.621	Type 2 DM with foot ulcer
E11.622	Type 2 DM with other skin ulcer
E11.628	Type 2 DM w/oth skin comp
E11.630	Type 2 DM w/periodontal disease
E11.638	Type 2 DM w/oth oral comp
E11.649	Type 2 DM w/hypoglycemia w/o coma
E11.65	Type 2 DM with hyperglycemia
E11.69	Type 2 DM w/oth spec complication
E13.618	Oth spec DM w/oth diab arthropathy
E13.620	Oth spec DM w/diabetic dermatitis
E13.621	Oth spec DM with foot ulcer
E13.622	Oth spec DM w/oth skin ulcer
E13.628	Oth spec DM w/oth skin comp
E13.630	Oth spec DM w/periodontal dz
E13.638	Oth spec DM w/oth oral comp
E13.649	Oth spec DM w/hypoglycemia w/o coma
E13.65	Oth spec DM with hyperglyemia
E13.69	Oth spec DM w/oth specified comp
E10.618	Type 1 DM w/oth diab arthropathy
E10.620	Type 1 DM w/diabetic dermatitis
E10.621	Type 1 DM with foot ulcer
E10.622	Type 1 DM with other skin ulcer

E10.628	Type 1 DM w/oth skin complication
E10.630	Type 1 DM w/periodontal disease
E10.638	Type 1 DM w/oth oral complication
E10.649	Type 1 DM w/hypoglycemia w/o coma
E10.65	Type 1 DM with hyperglycemia
E10.69	Type 1 DM w/oth spec complication
E11.69 & E11.65	Type 2 DM with other spec complication
E11.65	Type 2 DM with hyperglycemia
E10.69 & E10.65	Type 1 DM with other spec complication
E10.65	Type 1 DM wih hyperglycemia
E11.8	Type 2 DM w/uns complications
E13.8	Oth spec DM w/uns complications
E10.8	Type 1 DM w/unspec complications
E11.65	Type 2 DM with hyperglycemia
E11.8 & E11.65	Type 2 DM w/uns complications
E10.65	Type 1 DM with hyperglycemia
E10.8 & E10.65	Type 1 DM w/unspec complications

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