Diabetes Tests, Programs and Supplies

Number: 0070

(Includes CPB 121)

Policy
*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Note: Except for Medicare plans and where coverage is mandated by state law, generally coverage for diabetic supplies would be provided under a pharmacy rider and not as part of medical coverage. Certain diabetic supplies may also be covered under the medical plan if no pharmacy or diabetic supplies rider is available. Please check plan benefits.

I. Diabetes Self-Care Programs:

Aetna considers outpatient medical self-care programs medically necessary for persons with diabetes when such programs meet the following criteria:

A. The program consists of services of recognized healthcare professionals (e.g., physicians, registered dieticians, registered nurses, registered pharmacists); and
B. The program is designed to educate the member about medically necessary diabetes self-care; and
C. The program is ordered by the physician treating the
member's diabetes and includes a statement signed by the physician that the service is needed.

II. Diabetic Supplies:

The following diabetic supplies are considered medically necessary for persons with diabetes:

- Alcohol swabs;
- Blood glucose monitors;
- Blood glucose test strips;
- Control solutions;
- Insulin pens;
- Lancets;
- Needles and syringes for insulin administration; and
- Urine test tablets/strips.

Note: Coverage of diabetic supplies varies by medical and pharmacy plan. Please check plan documents for details.

III. Lasette™ Laser Blood Glucose Monitoring Device:

Aetna considers the Lasette laser blood glucose monitoring device (Cell Robotics International Inc., Albuquerque, NM), which uses a laser instead of a lancet to perforate the skin to obtain a blood sample for glucose measurement, experimental and investigational. There is insufficient evidence in the peer-reviewed medical literature that laser skin perforation offers clinically significant advantages over standard lancets.

IV. Glycated Serum Proteins (GSP):

Aetna considers devices to measure glycated serum proteins (fructosamine) (e.g., Duet™ Glucose Control System by LXN Corporation) experimental and investigational because the clinical utility of monitoring glycated serum proteins has not been established.
V. Glutamic Acid Decarboxylase (GAD) Autoantibodies:

Aetna considers measurement of autoantibodies to GAD medically necessary for distinguishing type 1 from type 2 diabetes when the clinical history is ambiguous and the results of testing will influence patient management. Measurement of anti-GAD antibodies is also considered medically necessary in diagnosing stiff-person syndrome. Anti-GAD antibody measurement is considered experimental and investigational for predicting the onset of diabetes and for all other indications.

VI. PreDX Test

Aetna considers the PreDx Test experimental and investigational because there is inadequate evidence in the published peer-reviewed clinical literature regarding its effectiveness.

VII. Jet Injectors:

Aetna considers jet injectors (e.g., Vita-Jet II, Advanta Jet, Freedom Jet, Medi-Jector EZ, Biojector 2000) medically necessary durable medical equipment (DME) when the member or the member’s caregiver is physically unable to use a conventional needle-syringe. The use of jet injectors for other reasons is considered a matter of preference and convenience.

VIII. I-Port:

Aetna considers the I-Port Injection Port (Patton Medical) a non-covered convenience item.

IX. Continuous Glucose Monitoring Devices:

Aetna considers the short-term (72 hours to one week) diagnostic use of continuous glucose monitoring devices medically necessary for persons with diabetes who
have either of the following problems in controlling blood glucose level, unresponsive to conventional insulin dose adjustment:

A. Hypoglycemia unawareness; or
B. Repeated hypoglycemia (less than 50 mg/dl) and hyperglycemia (greater than 150 mg/dl) at the same time each day.

Aetna considers the short-term (72 hours to one week) diagnostic use of continuous glucose monitoring devices medically necessary to diagnose primary islet cell hypertrophy (nesidioblastosis) or persistent hyperinsulinemic hypoglycemia of infancy (PHHI) (congenital hypoglycemia). in persons with symptoms suggestive of recurrent hypoglycemia.

For short-term (72 hours to one week) diagnostic use, no more than two continuous glucose monitoring periods are considered medically necessary within a 12-month period.

Aetna considers the long-term (greater than one week) therapeutic use of continuous glucose monitoring devices medically necessary as an adjunct to fingerstick testing of blood glucose in adults aged 25 years and older with type 1 diabetes, and for younger persons with type 1 diabetes who have had recurrent episodes of severe hypoglycemia (defined as two or more episodes of hypoglycemia (blood glucose less than 50 mg/dL) in a 30-day period with unawareness), despite appropriate modifications in insulin regimen and compliance with frequent self-monitoring (at least 4 fingersticks/day). Long-term use of continuous glucose monitoring devices is considered experimental and investigational for all other indications.

Aetna considers experimental and investigational the long-term (therapeutic) use of continuous glucose monitors for nesidioblastosis (primary islet cell hypertrophy) and for monitoring blood glucose in nondiabetic persons following
gastric bypass surgery because there is insufficient evidence of the clinical benefits of this approach for these indications.

X. Biostator® Artificial Pancreas:

Aetna considers the Biostator System, a device which functions as an artificial pancreas, experimental and investigational. There are insufficient data in the published peer-reviewed medical literature documenting the safety and effectiveness of the Biostator.

XI. Artificial Pancreas Device Systems:

Aetna considers a continuous glucose monitor and insulin pump with a low glucose suspend feature (e.g., MiniMed 630G) an equally acceptable alternative to a standard insulin pump and continuous glucose monitor for medically necessary indications.

Aetna considers a continuous glucose monitor and insulin pump with closed loop system (programmed to automatically adjust delivery of basal insulin based on continuous glucose monitor sensor glucose values) (e.g., MiniMed 670G) an equally acceptable alternative to a standard insulin pump and continuous glucose monitor for medically necessary indications.

XII. GlucoWatch® Biographer Monitor:

Aetna considers the GlucoWatch Biographer (Cygnus Inc, Redwood City, CA.), a glucose meter that is worn on the wrist, experimental and investigational.

XIII. Blood Glucose Meters for Persons with Visual Impairment:

Aetna considers reflectance meters with an electronic voice, automatic timers, and specially designed arrangements of supplies and materials to allow the visually impaired to use the equipment without assistance medically necessary DME
only for legally blind (best corrected visual acuity less than 20/200) persons with diabetes.

XIV. Blood Glucose Monitors with Integrated Lancing/Blood Sample:

Aetna considers blood glucose monitors with integrated lancing/blood sample medically necessary DME in persons with diabetes who meet either of the following criteria:

A. Persons who are legally blind (best corrected visual acuity less than 20/200); or
B. Persons with impairment of manual dexterity severe enough to require the use of this special monitoring system.

XV. Alternate Site Blood Glucose Monitors:

Aetna considers alternate site blood glucose monitors medically necessary DME for the following persons with diabetes, when an alternate site blood glucose monitor is recommended by their physician:

A. Children below age of 12 years; or
B. Persons who have used conventional blood glucose meters for at least 1 month (more than 30 days) and who have been non-compliant with blood glucose testing because of pain sensitivity or heavily callused fingertips.

Alternate site blood glucose monitors have no proven value over standard blood glucose monitors for other indications.

XVI. Home Glycated Hemoglobin Monitors:

Aetna considers home glycated hemoglobin (HbA1c or A1C) monitors (e.g., A1cNow Diabetes Monitor, Metrika Inc., Sunnyvale, CA) experimental and investigational. There are no prospective clinical studies demonstrating improvements
in compliance or other clinically significant benefits of home A1C testing over laboratory A1C testing. Individual-case exceptions to this policy may be made upon medical review for members who are unable to access laboratory A1C testing.

XVII. Diabetes Management Software

Aetna considers mobile application software (e.g., BlueStar) for self-management of diabetes experimental and investigational because its effectiveness has not been established.

*Note:* Aetna considers computer software for analyzing blood glucose monitor test results as an integral part of a blood glucose monitor and not separately reimbursed. In addition, software or hardware required for downloading data from a blood glucose monitor to a computer are considered an integral part of the blood glucose monitor and not separately reimbursed.

XVIII. Personal Digital Assistant-Based Blood Glucose Monitor:

Aetna considers a personal digital assistant-based blood glucose monitoring devices (e.g., TheraSense FreeStyle Tracker, Accu-Check Advantage Module) and module experimental and investigational because they have not been shown in published clinical studies to improve clinical outcomes over standard blood glucose monitors. (*Note:* A personal digital assistant (PDA) does not meet Aetna's definition of covered DME in that the PDA can be used in the absence of illness or injury).

XIX. Cellular Glucometry

*Note:* Aetna considers a feature that allows wireless transmission of blood glucose test results (cellular-enabled glucometer) as an integral part of the glucometer and not separately reimbursed.
XX. Disposable Blood Glucose Monitor:

Aetna considers a disposable blood glucose monitor (e.g., the ReliOn NewTek (Hypoguard USA, Inc., Edina, MN)) an acceptable medically necessary alternative to a standard blood glucose monitor.

XXI. Infrared Thermometer Device:

Aetna considers an infrared thermometer device (e.g., TempTouch) for the intermittent measurement and monitoring of skin surface temperature experimental and investigational because of insufficient evidence of its effectiveness in reducing the risk for diabetic foot ulceration.

XXII. Measurement of Advanced Glycation End Products by Skin Autofluorescence

Aetna considers measurement of advanced glycation end products by skin autofluorescence experimental and investigational because of insufficient evidence of its effectiveness compared to the oral glucose tolerance test.

XXIII. Remote Glucose Monitoring

Aetna considers remote wireless glucose monitoring devices (e.g., mySentry) experimental and investigational for managing persons with diabetes, as there is insufficient published evidence of the impact of remote glucose monitoring on clinical outcomes. Aetna does not cover an attachment to allow wireless transmission from a continuous glucose monitor to a smart phone or computer (e.g., MiniMed Connect) because it is considered a convenience feature. Aetna provides no additional reimbursement for a wireless transmission feature that is integrated into a continuous glucose monitor (e.g., Dexcom SHARE) because it is considered a convenience feature.

XXIV. Combinational Items
Aetna considers combination devices that include a home blood glucose monitor combined with a blood pressure monitor, cholesterol screening analyzer, or other devices (e.g., cellular telephone) not specifically indicated for the management of diabetes mellitus as not medically necessary convenience items.

XXV. Insulin Infusion Pumps:

For clinical policy on insulin infusion pumps, please see [CPB 0161 - Infusion Pumps](../100_199/0161.html).

XXVI. Hypoglycemic Wristband Alarm:

Aetna considers hypoglycemic wristband alarm (e.g., Sleep Sentry) a convenience item.

Background

*Diabetes Test Strips and Meters*

Diabetic test strips and meters are test strips and meters used for blood sugar testing. Once a blood sample has made it on to the glucose strip, a glucose meter device is used to measure the glucose in the blood. In each test strip, glucose oxidase reacts with the glucose in the blood sample to form gluconic acid. Diabetic test strips and meters are available in multiple brands. Examples of brand names include: Abbott Optium Plus; Abbott Freestyle; Accu-Chek Aviva; Accu-Chek Active; Accu-Chek Advantage; Accu Chek Compact; Bayer Contour; Bayer Contour NEXT; OneTouch Ultra; OneTouch Vita; and OneTouch Verio.

*Glycated Serum Proteins (Fructosamine)*

Aetna considers devices to measure glycated serum proteins (fructosamine) (e.g., Duet™ Glucose Control System by LXN Corporation) experimental and investigational. The fructosamine test measures the average of continuous glucose levels over the prior 2- to 3-week period, and is being marketed
as an indicator of overall glucose control in diabetics. The American Diabetes Association has determined that measurement of glycated serum protein (GSP) should not be considered the equivalent of measurement of glycated hemoglobin, and that the clinical utility of monitoring GSPs has yet to be established. A randomized clinical trial (Petitti et al, 2001) of 140 patients with diabetes found that patients randomized to home fructosamine monitoring had higher levels of glycated hemoglobin (HbA1c) after 3 and 6 months of follow-up. In a review of GSP and diabetes, Goldstein (1997) concluded that “further studies are recommended to determine whether the use of GSP to document short-term changes (e.g., 1 to 2 weeks) in glycemic status is clinically useful”.

Glutamic Acid Decarboxylase (GAD-65) Antibodies

Glutamic acid decarboxylase (GAD) is an enzyme that is produced primarily by pancreatic islet cells. A number of recent studies indicate that patients with type 1 diabetes often have antibodies to GAD and several other islet cell antigens. This is consistent with the hypothesis that type 1 diabetes is an autoimmune disease and that autoantibody production is an early step in the development of type 1 diabetes. Autoantibodies can be detected in many cases prior to the onset of glucose intolerance. The presence of GAD autoantibodies has been shown to be a strong predictive marker for the eventual onset of type 1 diabetes.

Measurement of anti-GAD antibodies has been proposed for evaluating the risk of developing type 1 diabetes in persons at high risk. However, the value of such testing is unproven, as there are no measures that have been demonstrated to be effective in preventing the onset of type 1 diabetes. Guidelines from the Canadian Diabetes Association (Ur et al, 2003) explain that the loss of pancreatic beta cells in persons who subsequently develop type 1 diabetes passes through a subclinical prodrome that can be detected reliably in first- and second-degree relatives of persons with type 1 diabetes by the
presence of anti-GAD antibodies and other pancreatic islet cell autoantibodies in their sera. While randomized trials testing prevention strategies have been completed or are now underway, safe and effective preventive strategies have not been identified. The guidelines concluded: "Therefore, any attempts to prevent type 1 diabetes should be undertaken only within the confines of formal research protocols."

Measurement of anti-GAD antibody can be of use in distinguishing type 1 from type 2 diabetes when the clinical history is ambiguous. Guidelines from the Royal Australian College of General Practitioners (RACGP, 2007) explained that measurement of GAD can be of particular use in diagnosing Late onset Autoimmune Diabetes in Adults (LADA), a form of late onset diabetes that is autoimmune and requires treatment with insulin within a relatively short period of time after diagnosis (often within the next 2 years). RACGP guidelines explained that persons with LADA tend to be young (30 to 40 years of age, lean, and have a personal and/or family history of other autoimmune diseases (e.g., hypo- or hyper-thyroidism). The guidelines stated that testing for GAD antibodies can confirm the diagnosis in ambiguous cases and prompt counseling the person about the likely time course of diabetes progression and the possibility of other autoimmune disease. In addition, the establishment of the LADA diagnosis may be useful in selecting therapy (Brophy et al, 2007)

Antibodies to GAD are often markedly elevated in patients with the stiff-person syndrome (also referred to as stiff-man syndrome), a condition that is associated with fluctuating stiffness and paroxysmal spasms of the trunk and legs.

PreDx Diabetes Risk Score

The PreDx® Diabetes Risk Score (DRS) test is a multiple-biomarker test to identify high-risk individuals who might develop diabetes within 5 years. Using a proprietary algorithm combines seven biomarkers to quantify the risk of developing diabetes within 5 years. The model also includes age and sex. A
diabetes risk score between 1 and 10 is calculated, with a higher score indicating an increased likelihood of developing diabetes within 5 years. Since the biomarkers are a combination of proteins and metabolites, they are measured using several different methods: ion-exchange high-performance liquid chromatography (HbA1c), chemiluminescent immunoassay (ferritin and interleukin 2 receptor alpha [IL2-Rα]), enzymatic (glucose), immuno-turbidometric assay (C-reactive protein [CRP]), and an enzyme-linked immunosorbent assay (adiponectin and insulin). The PreDx DRS is used for patients who do not have type 2 diabetes (T2D) but are at increased risk for developing this condition. Patients to be considered include those with impaired fasting glucose, metabolic syndrome, or other risk factors, including family history, age > 45 years, presence of obesity, coronary artery disease, hypertension, low high-density lipoprotein cholesterol (HDL) (i.e., < 35 milligrams per deciliter), increased triglycerides, and belonging to an ethnic group with a higher prevalence of diabetes (for example, African American, Hispanic, Asian or Native American).

Currently, two laboratories offer the PreDx DRS multibiomarker test. However, all testing is done at one of these facilities, Tethys Bioscience Inc.

Jet Injectors

Jet injectors offer an alternative method of hypodermic drug delivery from conventional needle-syringe. The main objective in using a jet injector as opposed to conventional needle-syringe is for increased patient comfort during injection. A review of the literature indicates some patients do prefer injection by jet injector while others may experience more discomfort. The Youth Task Force of the American Diabetes Association (Task Force on Jet Injections, 1998, 1991) reviewed the scientific literature on jet injection and could not make general recommendations for their use due to insufficient information. There are hypothetical risks and benefits associated with their use for insulin delivery which have not been clearly addressed in the literature. There is insufficient information on the frequency and significance of aversion to
needles, therefore, the use of jet injectors because of a fear of needles is a matter of convenience and patient preference. A jet injector may be appropriate for some individuals with medical conditions that make it impossible for them to use a conventional needle-syringe. Which group of patients unable to use syringes and who are therefore candidates for jet injections based on medical necessity has not been defined in the literature, but reasonably includes individuals with severe arthritis, severe tremors, or blindness.

I-Port Injection Port

The I-Port Injection Port (Patton Medical, Austin, TX) is an insulin delivery port which is used to reduce the number of needle injections of insulin. The I-Port is applied using an insertion needle to guide a soft cannula into the subcutaneous tissue. Once applied, the insertion needle is removed, leaving the soft cannula under the skin, acting as the gateway into the subcutaneous tissue. To inject through the I-Port, the needle of a syringe or insulin pen is used. The needle remains above the surface of the skin, while the medication is delivered through the soft cannula into the subcutaneous tissue. According to the manufacturer, the I-Port can accommodate 75 injections, and be worn for up to 72 hours. The I-Port was cleared by the U.S. Food and Drug Administration (FDA) based upon a 510(k) application.

In a prospective, randomized study, Blevins et al (2008) compared the I-Port to standard multiple dose insulin administration in diabetic patients receiving insulin injections (n = 74). Patients were randomly assigned to 2 of 3 treatment regimens: (i) standard injections (SI), (ii) a single I-Port device, or (iii) 2 separate I-Port devices (Dual I-Port). Each treatment regimen lasted 3 weeks and included 5 assessment visits. Patients in the single I-Port regimen injected both regular human or rapid-acting insulin and insulin glargine through the same device, whereas patients in the Dual I-Port regimen injected each type of insulin through 2 separate devices. Of the 74 patients who qualified to participate in the study, 64 (86 %)
completed all 5 assessment visits. Six of the 10 patients (8.1 %) who did not complete the trial terminated for device-related reasons (e.g., adhesive failure, wear discomfort, high blood glucose levels, cannula bends) and 4 patients (5.4 %) terminated for non-device-related reasons. The authors reported that 69.4 % of the patients found the I-Port useful and helpful in the management of their diabetes and there was no significant difference in patient’s glycosylated albumin between SI, single I-Port, and Dual I-Port treatment regimens.

In a systematic review of adherence with medications for diabetes, Cramer (2004) found a lack of studies evaluating interventions to improve adherence in which adherence was measured using appropriate methods. Cramer stated, "Further research is needed to quantify the specific improvement in glycemic control that might be obtained from improved medication adherence. Such studies should demonstrate the health benefits that may be derived from more convenient therapeutic regimens that are being developed for diabetes."

There is a lack of studies demonstrating an improved health benefit of the I-Port over standard injection regimens. Clinical studies are necessary to evaluate the I-Port's impact on compliance and other clinical outcomes.

**Continuous Glucose Monitors (CGMs)**

Continuous glucose monitoring systems (CGMS) are devices that measure glucose levels in interstitial fluid at programmable intervals. These readings, used along with fingerstick results, help detect any patterns or trends with an individual’s glucose levels and are intended to assist in calculating the insulin dosage needed to manage glycemic control. CGMS readings are intended to supplement, not replace, fingersticks.

CGMS use sensors that are inserted under the skin in the abdomen and work by extracting glucose from the interstitial fluid, measuring and recording the glucose level and converting these measurements into equivalent blood glucose readings.
Sensors are designed to be worn three to seven days, depending on the product. Calibration is required whenever a new glucose sensor is inserted, which requires obtaining blood glucose from a traditional fingerstick sample.

MiniMed Continuous Subcutaneous Glucose Monitoring System is an example of a diagnostic continuous glucose monitor for short-term use. The FDA granted the MiniMed CGMS (Medtronic MiniMed, Minneapolis, MN) pre-market approval in June 1999 for use as an adjunct to finger-stick blood glucose testing. CGMS that uses a recorder and subcutaneously implanted glucose sensor to store data to be downloaded to a personal computer. The system provides continuous measurements of the interstitial glucose levels that range from 40 to 400 mg/dl. The glucose sensor signal is acquired every ten seconds. An average of the acquired signals is saved in memory every five minutes for up to 3 days. While in operation, the MiniMed CGMS monitor does not display glucose values, and individuals are still required to test their glucose levels several times a day by a standard method (finger sticks) and enter the glucose measurements into the monitor for calibration purposes. The system is used as a diagnostic tool to evaluate glucose levels over a three day period and is then returned to the physician for evaluation of results to potentially modify diabetes treatment regimens and is not intended for long-term use. According to the FDA, the MiniMed CGMS is not intended to replace standard finger-stick testing. The newest short-term CGMS version of the MiniMed is the iPRO2.

More recently, the FDA approved the Guardian Real-Time (RT) Continuous Glucose Monitoring System (Medtronic, Minneapolis, MN), which is described by the manufacturer as the first consumer continuous glucose monitoring device. The Guardian CGMS device uses a glucose sensor connected to a transmitter that sends glucose readings every five minutes to a monitor. The glucose sensor is typically discarded and replaced after three days. According to the manufacturer, the device provides up to 288 glucose readings per day or every 5 minutes. Unique features include predictive and rate of change alarms.
and expanded trend graphs. Graphs can show the effect of exercise, diet, and lifestyle, as well as medication on glucose values using 3, 6, 12 and 24-hour increments. Alarms that signal high and low glucose alerts warn individuals of any significant glucose changes. Data is downloaded using the Medtronic Carelink Therapy Management Software. According to the FDA-approved labeling, the Guardian RT is indicated to supplement blood glucose information from standard home blood glucose meters, for persons 7 years and older with type 1 or type 2 diabetes. A fingerstick measurement is required before taking action.

The DexCom STS Continuous Glucose Monitoring System (DexCom, Inc., San Diego, CA) gained FDA approval on March 24, 2006. It is a glucose sensor that reports glucose values every 5 minutes for up to 72 hours. These readings are used with fingerstick results to detect trends and patterns in glucose levels in adults with diabetes, aged 18 years and over. The DexCom STS is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices.

The Dexcom G4 PLATINUM (adult and pediatric) Systems with Share is a CGMS that incorporates a sensor, transmitter and receiver and allows glucose to be monitored every five minutes. The sensor reports glucose for seven days before a new sensor replacement is necessary. A built-in alarm system can be programmed by the user when glucose falls below a pre-set low and a pre-set high level. A built-in hypoglycemia safety alarm alerts user when glucose hits 55 mg/dl. FDA approved for use in adults and children ages 2 years and older. Dexcom Share is an integrated wireless communication system that is built into the receiver, enabling remote monitoring capabilities and sharing of data through a compatible internet-accessible device application.

The Dexcom G5 Mobile CGM System is described as a complete, mobile CGMS with wireless technology that is built into the transmitter. Glucose information is sent wirelessly from the
device transmitter to a compatible smart device or Dexcom G5 receiver. FDA approved for use in adults and children ages 2 years and older.

Combined external insulin pumps with CGMS are devices that integrate an insulin pump with real-time continuous glucose monitoring and is not intended to replace finger sticks. These systems incorporate features including predictive alerts that give early warnings so action can be taken to prevent dangerous high or low blood glucose events.

The Paradigm Real Time System (Medtronic MiniMed) is an open-loop insulin delivery system that combines an external insulin pump with continuous monitoring of interstitial glucose levels via a subcutaneous sensor. The sensor communicates glucose readings to the pump using a radio transmitter. The pump can also calculate recommended insulin doses, which the patient can accept or modify. Readings from the continuous glucose monitor (CGM) are not intended to be used to make therapy adjustments. A conventional blood glucose meter reading is needed before making adjustments because there is a lag of up to 10 minutes in glucose concentration in the interstitial fluid relative to the concentration in the blood (CADTH, 2007). Furthermore, readings from the sensor may be less accurate in the hypoglycemic range. An assessment of the Paradigm Real Time System by the Canadian Agency for Drugs and Technologies in Health (CADTH, 2007) concluded: "Based on the limited amount of research published to date, the impact of the Paradigm Real-Time System on long-term glycemic control, prevention of diabetic complications, or quality of life is unclear." The assessment noted that open-loop systems such as the Paradigm Real Time System are an incremental step towards a fully closed-loop system, also known as an artificial pancreas, where insulin dosages would be automatically adjusted, rather than requiring patient input.

The MiniMed Paradigm REAL-Time Revel System is approved for use in adults and children ages 7 years and older and works with the my Sentry remote monitoring system. The mySentry
remote monitoring system is an optional monitoring device for the MiniMed Paradigm REAL-Time Revel System. The mySentry consists of a remote outpost and monitor. Blood glucose levels collected by the CGM are sent to the remote (wireless) monitor, which also has alarms to alert the user of high or low blood glucose levels.

The Animas Vibe System combines a Dexcom G4 Platinum sensor and transmitter with the Animas Vibe insulin pump. It is FDA approved for use in adults and children, ages 2 years and older.

Guidelines from the National Institute for Health and Clinical Excellence (2004) recommended the use of CGM devices for the evaluation of persons with type 1 diabetes on insulin therapy who have repeated hypoglycemia and hyperglycemia at the same time each day, and hypoglycemia unawareness, unresponsive to conventional insulin dose adjustment.

A Cochrane systematic evidence review found limited evidence for the effectiveness of real-time continuous glucose monitoring (CGM) use in children, adults and patients with poorly controlled diabetes (Miranda, et al., 2012). The authors found that the risk of severe hypoglycemia or ketoacidosis was not significantly increased for CGM users, but as these events occurred infrequent these results have to be interpreted cautiously.

A multi-center randomized clinical study sponsored by the Juvenile Diabetes Research Foundation (JDRF, 2008) provided evidence of improved glycemic control over the intermediate term (6 months) with the use of CGMs in adults greater than 24 years of age. In this study, 322 adults and children who were already receiving intensive therapy for type 1 diabetes were randomly assigned to a group with continuous glucose monitoring or to a control group performing home monitoring with a blood glucose meter. All subjects were stratified into 3 groups according to age and had a glycated hemoglobin level of 7.0 to 10.0 %. The investigators found that the changes in
glycated hemoglobin levels in the 2 study groups varied markedly according to age group, with a significant benefit in patients 25 years of age or older with continuous glucose monitoring (mean difference in change, −0.53 %, p < 0.001). There was no significant benefit in glycated hemoglobin levels with continuous glucose monitoring in subjects who were 15 to 24 years of age (mean difference, 0.08; p = 0.52) or among those who were 8 to 14 years of age (mean difference, −0.13; p = 0.29). The investigators posited that the disparate outcomes may be due to poorer compliance among younger age groups. The use of continuous glucose monitoring averaged 6.0 or more days per week for 83 % of patients 25 years of age or older, 30 % of those 15 to 24 years of age, and 50 % of those 8 to 14 years of age. The study also found no significant difference in the rate of severe hypoglycemia among persons who were assigned to CGMs and those who performed home monitoring with a blood glucose meter; however, the investigators noted that the trial was not powered to detect such a difference. Commenting on the JDRF study of continuous glucose monitoring, Brett (2008) noted that "although this method is appealing theoretically, the extent to which it will improve long-term clinical outcomes remains to be determined."

A controlled clinical study, the Sensor-Augmented Pump Therapy for A1C Reduction (STAR) 3 trial, found that, in both adults and children with inadequately controlled type 1 diabetes, sensor-augmented pump therapy resulted in significant improvement in glycated hemoglobin levels, as compared with injection therapy (Bergenstal, et al., 2010). However, whether these results can be translated into community practice outside of the controlled clinical trial setting is unknown. A 1-year, multi-center, randomized, controlled trial, compared the efficacy of sensor-augmented pump therapy (pump therapy) with that of a regimen of multiple daily insulin injections (injection therapy) in 485 patients (329 adults and 156 children) with inadequately controlled type 1 diabetes. Patients received recombinant insulin analogs and were supervised by expert clinical teams. The primary end point was the change from the baseline
glycated hemoglobin level. At 1 year, the baseline mean glycated hemoglobin level (8.3 % in the 2 study groups) had decreased to 7.5 % in the pump-therapy group, as compared with 8.1 % in the injection-therapy group (p < 0.001). The proportion of patients who reached the glycated hemoglobin target (less than 7 %) was greater in the pump-therapy group than in the injection-therapy group. The rate of severe hypoglycemia in the pump-therapy group (13.31 cases per 100 person-years) did not differ significantly from that in the injection-therapy group (13.48 per 100 person-years, p = 0.58). There was no significant weight gain in either group. A commentator noted that this is a manufacturer-sponsored study, and the investigators included employees of the firm. An editorialist (Wolpert, 2010) offered several caveats: These patients received intensive support and monitoring that are not available to many patients, were highly skilled at self-management before enrollment, and had to be adept at calibration and management of equipment failures and alarms. The editorialist warned that the "expert training and guidance [on the use of continuous glucose monitoring] received by patients in clinical trials cannot be readily duplicated in a busy clinical practice." A commentary (Schwenk, 2010) concluded: "This new and expensive technology must be tested in wider community-based trials before it will be ready for broad dissemination."

The editorialist (Wolpert, 2010) also compared the results of the STAR-3 trial with the JDRF trial, and stated that the differences in outcome may be due to differences in the design of these trials. In the STAR 3 study, the patients in the pump-therapy group changed their mode of both insulin delivery and glucose monitoring at the time of randomization, whereas in the JDRF trial, patients who were assigned to receive continuous glucose monitoring did not change their mode of insulin delivery. The editorialist stated that the greater reduction in glycated hemoglobin levels among adult patients in the STAR 3 trial than in the JDRF study may reflect the additional effect of initiating pump therapy, as well as the increased baseline glycated hemoglobin levels in the STAR 3
study, as compared with the JDRF study (8.3% and 7.6%, respectively).

The editorialist (Wolpert, 2010) also noted that, in the STAR 3 study, the improved glycemic control among children in the pump-therapy group contrasted with the lack of apparent benefit for continuous glucose monitoring among children in the JDRF trial. The editorialist questioned whether the benefits that were seen in the pump-therapy group in the STAR 3 study were due primarily to the initiation of pump therapy rather than to continuous glucose monitoring. The editorialist explained that consistent with this possibility is the fact that patients in the STAR 3 study who had a relatively low frequency of sensor use had significant improvements in glycated hemoglobin levels. The editorialist noted that children in the injection-therapy group, who used intermittent capillary blood glucose monitoring, had lower rates of both severe and biochemical hypoglycemia than did patients in the JDRF trial who used continuous monitoring. The editorialist said that these results suggest that the selection of patients may also account for some of the differences in the outcomes of these two trials.

Whether the benefits of CGM in improving glycemic control extend beyond the intermediate-term (12 months) is unknown. A large clinical study of CGM, the Minimally Invasive Technology Role and Evaluation (MITRE) study, sponsored by the National Institute for Health Research Health Technology Assessment Program, found that continuous blood glucose monitoring had no durable effect on blood glucose control (Newman et al., 2007; Newman et al, 2009). The purpose of the MITRE study was to evaluate the efficacy of minimally invasive glucose monitoring devices in 400 patients with diabetes mellitus treated with insulin. The primary endpoint was long-term glucose control, as indicated by changes in glycosylated hemoglobin (HbA1c) levels for 18 months. A total of 400 patients were randomly assigned to the CGMS by MiniMed, the Biographer by Animas, a standard control or to an attention control group. Mean baseline HbA1c ranged from 7.0% to 15.5
% for participants. All groups demonstrated a decline in mean HbA1c, especially during the first few months of the study. However, by month 18, the percentage of patients that had a relative reduction of at least 12.5 % was 15 % in the Biographer group, 27 % in the CGMS group, 24 % in the standard control, and 27 % in the attention control group. The relative decline in HbA1c from baseline ranged from 1 % to 4.6 %. The results suggested that the use of the CGMS had a small benefit, but only in the short-term, and that the Biographer had less impact on HbA1c than either the CGMS or standard treatment. The assessment concluded: "Continuous glucose monitors as assessed in this study do not lead to improved clinical outcomes and are not cost-effective for improving HbA1c in unselected individuals with poorly controlled insulin-requiring diabetes" (Newman et al, 2009). Some commentators have posited that more advanced continuous glucose monitoring devices currently in use may provide more durable results than the monitors used in the MITRE study. The results from CGMs used in this study were downloaded and reviewed with the endocrinologist, but only the Glucowatch Biographer provided real-time display of glucose results to the patient (the MiniMed CGMS used in this study did not include a real-time display of glucose readings). Whether the more advanced CGMs with real-time display will provide more durable results than earlier models used in the MITRE study is a question for future long-term studies.

Nørgaard et al (2013) reported on the largest and longest multicenter prospective observational study of continuous glucose monitoring with insulin infusion pumps, so called sensor-augmented pump therapy. The investigators reported on a 12-month observational study in patients with type 1 diabetes treated with continuous subcutaneous insulin infusion (CSII), upon the introduction of continuous glucose monitoring (CGM). The study was conducted in 15 countries to document the real-life use of sensor-augmented pump therapy and assess which variables are associated with improvement in type 1 diabetes management. Data from 263 patients (38% male; mean age, 28.0±15.7 years [range, 1-69 years]; body mass
index, 23.3±4.9 kg/m²; diabetes duration, 13.9±10.7 years; CSII duration, 2.6±3 years) were collected. Baseline mean glycated hemoglobin A1c (HbA1c) was 8.1±1.4%; 82% had suboptimal HbA1c (≥7%). The investigators found that the average sensor use for 12 months was only 30% (range, 0-94%), and that sensor use decreased with time (first 3 months, 37%; last 3 months, 27%). The investigators found that there were significantly more patients with an HbA1c value of < 7.5% after 3 months of sensor-augmented pump therapy than at baseline (baseline, 29%; 3 months, 37%) However, the percentage of patients with an HbA1c value of < 7.5% decreased over the 12-month observation period, such that the percentage of patients with an HbA1c value of < 7.5% after 12 months was not statistically significantly higher than at baseline.

A published systematic evidence review and meta-analysis of the evidence for continuous glucose monitoring systems in children with type 1 diabetes reached the following conclusions (Golicki et al, 2008): "The Continuous Glucose Monitoring System is not better than self-monitoring of blood glucose with regard to improvement of metabolic control among type 1 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."

Chetty et al (2008) of McMaster University performed a meta-analysis of randomized controlled trials comparing continuous glucose monitoring and self-blood fingerstick glucose monitoring in persons with type 1 diabetes. The investigators found insufficient evidence to support the notion that CGM provides a superior benefit over self-blood fingerstick glucose monitoring in terms of hemoglobin A1c reduction. The investigators, however, found some indication of improved detection of asymptomatic nocturnal hypoglycemia in the CGM group. The investigators identified 7 studies with a total of 335 patients fulfilled the inclusion criteria. Five studies were confined to the pediatric population (age less than 18 years). Study duration varied from 12 to 24 weeks. The investigators
found that, compared with self-blood fingerstick glucose monitoring, CGM was associated with a non-significant reduction in hemoglobin A1c (0.22 %; 95 % confidence interval [CI]: -0.439 % to 0.004 %, p = 0.055).

Regarding the therapeutic use of continuous glucose monitoring devices for hypoglycemic unawareness, current evidence from randomized controlled clinical trials have focused on CGM's effect on shortening the duration of asymptomatic hypoglycemia, an intermediate endpoint, rather than clinical outcomes. The clinical significance of reductions in duration of asymptomatic hypoglycemia are unknown. In addition, current evidence indicates that continuous glucose monitoring devices are least accurate in the hypoglycemic range (CADTH, 2007; Melki et al, 2006).

Hypoglycemia unawareness is reversible. Meticulous avoidance of hypoglycemia for several weeks is sufficient to restore awareness of hypoglycemia (Cheng et al, 2000; Fanelli et al, 1993; Dagogo-Jack et al, 1994; Cranston et al, 1994). The return of awareness is accomplished with minimal compromise of glycemic control, but that required substantial involvement of health professionals. In addition, unlike CGM, HAATT/BGAT (Hypoglycemia Anticipation, Awareness and Treatment Training/ Blood Glucose Awareness Training) has been proven to reduce the occurrence of severe hypoglycemia (Cox et al, 2001; Cox et al, 2004).

There is limited evidence of the effectiveness of CGMs to improve outcomes in pregnant women with diabetes. Murphy et al (2008) reported on an open-label randomized controlled clinical trial where 71 pregnant women with type 1 diabetes (n = 46) or type 2 diabetes (n = 25) were randomly assigned to antenatal care plus continuous glucose monitoring (n = 38) or to standard antenatal care (n = 33). Continuous glucose monitoring was used as an educational tool to inform shared decision making and future therapeutic changes at intervals of 4 to 6 weeks during pregnancy. All other aspects of antenatal care were equal between the groups. Women randomized to
continuous glucose monitoring had lower mean hemoglobin A1c levels (5.8 %) from 32 to 36 weeks’ gestation compared with women randomized to standard antenatal care (6.4 %). Compared with infants of mothers in the control arm those of mothers in the intervention arm had decreased mean birthweight standard deviation scores (0.9 versus 1.6), decreased median customized birthweight centiles (69 % versus 93 %), and a reduced risk of macrosomia (odds ratio 0.36). The investigators noted a number of limitations to this study. Although efforts were made to standardize antenatal contacts between groups, health professionals were not blinded and therefore the possibility of bias in clinical management cannot be excluded. Differences in maternal characteristics, with longer duration of diabetes in the intervention group, may have contributed to some of the effect on infant outcomes. The investigators stated that the study included a small number of women and that larger multicenter trials are required to assess the impacts of continuous glucose monitoring in pregnancy.

Guidelines from the American Diabetes Association (2009) state that continuous glucose monitoring in conjunction with intensive insulin regimens can be a useful tool to lower hemoglobin A1c in selected adults (aged greater than 25 years) with type 1 diabetes (A -- recommendation based upon evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered. The guidelines state that, "although the evidence for [hemoglobin] A1C lowering is less strong in children, teens, and younger adults, continuous glucose monitoring may be helpful in these groups. Success correlates with adherence to ongoing use of the device" (C -- recommendation based upon evidence from poorly controlled or uncontrolled studies). The ADA guidelines (2009) stated that continuous glucose monitoring "may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes" (E -- recommendation based upon expert consensus or clinical experience). The guidelines stated that this recommendation is based upon expert opinion rather than clinical studies. ADA guidelines (2008) explained: "In recent years, methods to
sample interstitial fluid glucose (which correlates highly with blood glucose) in a continuous and minimally invasive way have been developed. Most microdialysis systems are inserted subcutaneously, while an early system employed “reverse iontophoresis” to move glucose across the skin. The concentration of glucose is then measured by a glucose oxidase electrode detector. These systems require calibration with SMBG readings, and the latter are still recommended for making treatment decisions. Continuous glucose sensors have alarms for hypo- and hyperglycemia. Small studies in selected patient populations have shown good correlation of readings with SMBG and decreases in the mean time spent in hypo- and hyperglycemic ranges compared with blinded sensor use. Although continuous glucose sensors would seem to show great promise in diabetes management, as yet no rigorous controlled trials have demonstrated improvements in long-term glycemia."

A structured review of the evidence conducted by the BlueCross BlueShield Association Technology Evaluation Center (2003) concluded that “use of intermittent or continuous interstitial fluid glucose monitoring in patients with diabetes mellitus does not meet Blue Cross and Blue Shield Association Technology Evaluation Center criteria.” Similarly, a technology assessment conducted by the California Technology Assessment Forum (CTAF) concluded that continuous glucose monitoring does not meet CTAF’s criteria (Tice, 2003). An updated assessment of continuous glucose monitoring by the California Technology Assessment Forum (Karliner, 2009) concluded that continuous glucose monitoring devices meet CTAF criteria for use in type 1 diabetes mellitus in non-pregnant adults requiring multiple (greater than or equal to 3) daily insulin injections and frequent (greater than or equal to 3) self-monitoring blood glucose checks. Continuous glucose monitoring devices did not meet CTAF criteria 3 for the management of type 1 diabetes mellitus in children, adolescents and pregnant women. The CTAF assessment explained that the largest randomized controlled clinical trial to date of continuous glucose monitoring devices for adults and children (citing JDRF, 2008) found
conclusive benefit only for adults 25 years and older. The CTAF assessment explained that, while in this study, and in other smaller randomized controlled trials there is evidence that both children and adults spend less time in a hypoglycemic glucose range when using a continuous glucose monitoring device compared to usual care frequent SMBG, there is little evidence that use of a continuous glucose monitoring device confers an ultimate health benefit as measured by HbA1C as a marker of overall glycemic control. The CTAF assessment stated that it may be that for children and adolescents this is in large part due to difficulty with device adherence and not with the device itself. The CTAF assessment explained, however, that a health technology is only as good as its actual clinical application, and the evidence has not yet shown conclusive benefit for children, adolescents, and even young adults. Likewise, while the small studies that exist of pregnant women show the feasibility of continuous glucose monitoring device use during pregnancy, they do not yet demonstrate conclusive benefit in this population either. The CTAF assessment concluded that future study of these devices should incorporate more research on how the devices can be made more acceptable and user-friendly for children and adolescents with type 1 diabetes in order to optimize potential clinical benefit for this population. The CTAF assessment also stated that larger studies of pregnant women which are limited to those women requiring multiple insulin injections per day are needed in order to adequately assess potential benefit in this population.

A technology assessment of self-monitoring of blood glucose in persons with type 2 diabetes prepared for the Centers for Medicare and Medicaid Services (Balk et al, 2006) commented that “currently, CGM [continuous glucose monitoring] has been studied primarily in children with type 1 diabetes. It is unclear whether CGM provides added value to traditional SMBG [self monitoring of blood glucose].”

Available evidence shows that, in contrast to type 1 diabetes, persons with type 2 diabetes do not benefit from tight glucose control. In 3 recent large randomized trials (ACCORD,
ADVANCE, 3 and VADT4), tight control in patients with long-standing type 2 diabetes did not lower overall mortality, cardiovascular-related mortality, stroke, amputations, or even clinical (as opposed to surrogate) microvascular endpoints (Gerstein et al, 2008; Patel et al, 2008; Duckworth et al, 2009). Some authorities suggested that the HbA1c goals for practice guidelines should not be less than 7 % and that, to encourage individualized treatment, performance measures should set an upper limit (e.g., 9 %) rather than a lower limit (e.g., less than 7 %) (Lehman and Krumholz, 2009).

A Cochrane systematic evidence review found that intensive glucose control significantly prevents the development of clinical neuropathy in type 1 diabetes mellitus (Callaghan, et al., 2012). However, in type 2 diabetes mellitus, the effect of intensive glucose control on the incidence of clinical neuropathy was not statistically significant. The systematic evidence review also found that intensive glucose control significantly increases the risk of severe hypoglycemic episodes, which needs to be taken into account when evaluating its risk/benefit ratio.

A systematic evidence review of continuous glucose monitoring by the Ontario Ministry of Health and Long-Term Care Medical Advisory Secretariat (MAS, 2011) found that there was moderate quality evidence that in diabetic individuals with an infusion pump, continuous blood glucose monitoring plus self-monitoring was not more effective in reducing glycosylated hemoglobin, hypoglycemic events or severe hypoglycemic events than self-monitoring alone.

A systematic evidence review prepared for the Agency for Healthcare Research and Quality (Golden, et al., 2012) reported that randomized controlled trials showed no difference in the effect of CSII and MDI on HbA1c (moderate strength of evidence [SOE]) or severe hypoglycemia (low SOE) for children or adolescents with type 1 diabetes, or for adults with type 2 diabetes. In adults with type 1 diabetes, HbA1c decreased more with CSII than with MDI (low SOE), but results were heavily
influenced by one study. The assessment found that there was no difference in severe hypoglycemia (low SOE). In children and adults with type 1 diabetes, CSII use was associated with improved quality of life compared with MDI (low SOE). There was insufficient evidence about quality of life for adults with type 2 diabetes. The SOE regarding pregnant women with pre-existing diabetes was either low or insufficient on all outcomes.

A systematic evidence review (Coca, et al., 2012) found that intensive glucose control reduced the risk for microalbuminuria and macroalbuminuria in persons with type 2 diabetes, but evidence was lacking that it reduced the risk of significant clinical renal outcomes, such as doubling of the serum creatinine level, end-stage renal disease or death from renal disease during the years of follow-up of the trials.

A review of continuous glucose monitors in type 2 diabetes by Meade (2012) stated that only five of the studies reviewed documented a reduction in HbA1c, and of these five, only three focused exclusively on patients with type 2 diabetes. The review stated that the majority of the studies evaluating CGM use in patients with type 2 diabetes were not designed to show a reduction in HbA1C. Studies of patients with type 2 diabetes mellitus had a smaller sample size than the studies reviewing continuous glucose monitoring in patients with type 1 diabetes.

Evidence to support the use of continuous glucose monitoring in persons with diabetes not on insulin is very limited. Vigersky, et al. (2011) reported on a randomized controlled trial of 100 adults with type 2 diabetes who were not on prandial insulin. This study compared the effects of 12 weeks of intermittent continuous glucose monitoring with self-monitoring of blood glucose (SMBG) on glycemic control over a 40-week follow-up period. Subjects received diabetes care from their regular provider without therapeutic intervention from the study team. The investigators reported that there was a significant difference in A1C at the end of the
3-month active intervention that was sustained during the follow-up period. The mean, unadjusted A1C decreased by 1.0, 1.2, 0.8, and 0.8% in the continuous glucose monitoring group vs. 0.5, 0.5, 0.5, and 0.2% in the SMBG group at 12, 24, 38, and 52 weeks, respectively (p = 0.04). There was a significantly greater decline in A1C over the course of the study for the continuous glucose monitoring group than for the SMBG group, after adjusting for covariates (p < 0.0001). The subjects who used continuous glucose monitoring per protocol (≥48 days) improved the most (p < 0.0001). The investigators reported that the improvement in the continuous glucose monitoring group occurred without a greater intensification of medication compared with those in the SMBG group.

Ehrhardt, et al. (2010) evaluated the utility of short-term use of continuous glucose monitoring in people with type 2 diabetes on a variety of treatment modalities except prandial insulin. The investigators conducted a prospective, 52-week, two-arm, randomized trial comparing real-time continuous glucose monitoring (RT-CGM) (n = 50) versus self-monitoring of blood glucose (SMBG) (n = 50) in people with type 2 diabetes not taking prandial insulin. Real-time continuous glucose monitoring was used for four 2-week cycles (2 weeks on/1 week off). All patients were managed by their usual provider. Mean (± standard deviation) decline in A1C at 12 weeks was 1.0% (± 1.1%) in the RT-CGM group and 0.5% (± 0.8%) in the SMBG group (p = .006). There were no group differences in the net change in number or dosage of hypoglycemic medications. Those who used the RT-CGM for ≥48 days (per protocol) reduced their A1C by 1.2% (± 1.1%) versus 0.6% (± 1.1%) in those who used it <48 days (p = .003). Multiple regression analyses statistically adjusting for baseline A1C, an indicator for usage, and known confounders confirmed the observed differences between treatment groups were robust (p = .009). There was no improvement in weight or blood pressure. Limitations of this study were the short duration (12 weeks) for the primary endpoint (52-week results were not reported), the atypical short-term use of CGM, the fact that person assigned to CGM tested their blood glucose more
frequently than persons assigned to SMBG, and the lack of other self-care data that may explain difference between groups.

There is some evidence to support the short-term diagnostic use of CGMs by medical professionals to detect unrecognized hypoglycemia, particularly unrecognized nocturnal hypoglycemia, in persons with type 2 diabetes. Chico et al (2003) reported on the diagnostic yield of the professional CGMs in persons with type 1 (n = 40) and type 2 diabetes (n = 30). The investigators reported that continuous glucose monitoring detected unrecognized hypoglycemas in 62.5 % of the type 1 diabetic patients and in 46.6 % of the type 2 diabetic patients. The investigators noted that 73.7 % of all unrecognized hypoglycemic events occurred at night.

Tanenberg et al (2004) reported on a randomized controlled trial evaluating the effect of continuous glucose monitoring in 128 subjects with insulin-treated diabetes; 10 subjects were diagnosed with type 2 diabetes. Subjects were randomly assigned to insulin therapy adjustments based on either professional continuous glucose monitoring or self-monitoring of blood glucose values. At the end of the study, patients in both groups used the CGM for 3 days; these values were used to calculate measures of hypoglycemia. Subjects assigned to continuous glucose monitoring had a significantly shorter duration of hypoglycemia (sensor glucose less than or equal to 60 mg/dL) at week 12 of the study (49.4 +/- 40.8 versus 81.0 +/- 61.1 minutes per event, p = 0.009). The small number of subjects with type 2 diabetes in this study do not allow reliable conclusions to be made about the impact of continuous glucose monitoring in this subgroup. Other limitations of the study include its short duration and the use of an outcome, duration of hypoglycemia, of uncertain clinical significance. It should be noted that, in both this study by Tannenberg et al (2004), and the study by Chico et al (2003) described above, continuous glucose monitoring was reported to have no significant effect on glycemic control as measured by hemoglobin A1c.
Hay et al (2003) reported on the incidence of hypoglycemia and hypoglycemia detected by short-term (72-hour) continuous glucose monitoring in 25 elderly persons (greater than 65-year old) with type 2 diabetes treated with a sulfonylurea who were well controlled (hemoglobin A1c less than 7.5 %). Elderly patients with type 2 diabetes were recruited if their glycosylated hemoglobin (HbA1c) was less than 7.5 % and if their oral hypoglycemic therapy included a sulfonylurea. Patients underwent 2 consecutive 72-hour periods of continuous glucose monitoring at baseline and then again at 1 month. Patients were asked to record 4 self-monitored capillary blood glucose levels each day for calibration of the monitor and also to record meal times, exercise, and symptoms of hypoglycemia. The number of hyperglycemic (greater than 144 mg/dL), hypoglycemic (less than 50 mg/dL), and borderline-hypoglycemic (50 to 65 mg/dL) events were determined (an event was defined as a glucose value that persisted for at least 15 mins with or without symptoms). Twenty-five patients (21 men, 4 women) 73.9 +/- 4.4 years old with an HbA1c of 6.2 +/- 0.8 % were each monitored for an average of 187.57 hrs. The mean glucose values were: fasting, 139 +/- 40 mg/dL; 2 hrs post-breakfast, 167 +/- 58 mg/dL; 2 hrs post-lunch, 157 +/- 53 mg/dL; and 2 hrs post-dinner, 149 +/- 49 mg/dL. Twenty patients (80 %) experienced a total of 103 hypoglycemic events (less than 50 mg/dL), and 14 of these patients experienced 54 events where the glucose levels were less than or equal to 40 mg/dL. Twenty-four patients (96 %) experienced borderline-hypoglycemia (50 to 65 mg/dL) (n = 229 events). Patients experienced a mean of 0.62 +/- 0.72 episodes of hypoglycemia (interstitial glucose less than 50 mg/dL) per day (4 to 5 episodes overall), 0.35 +/- 0.6 episodes per day where the interstitial glucose was less than or equal to 40 mg/dL (2 to 3 episodes overall), and 1.37 +/- 1.22 episodes of borderline-hypoglycemia (9 to 10 episodes overall). Each episode of hypoglycemia persisted for 78 +/- 73 mins, and borderline-hypoglycemia for 45 +/- 11 mins. Patients were hypoglycemic 3.3 % of the time and borderline-hypoglycemic 3.7 % of the time. No episode of hypoglycemia was recorded by any patient in his or her daily diary. High post-prandial
glucose values (greater than 144 mg/dL 2 hrs post-prandial) were recorded after 57 % of all meals (breakfast 60 %, lunch 57.5 %, dinner 55.2 %). The CGM was generally well-tolerated, but 52 % of patients could not be studied for the full 12 days of monitoring. The investigators reported that hypoglycemia and excessive post-prandial glycemic excursions are common in well-controlled patients with type 2 diabetes treated with a sulfonylurea with or without metformin. Limitations of the study included the fact that it was limited to persons on oral hypoglycemics, and that the study did not evaluate the impact of continuous glucose monitoring on improvements in clinical outcomes.

Zick et al (2007) reported on the yield of 72-hr continuous glucose monitoring versus self-monitoring of blood glucose in detecting hypoglycemia (less than or equal to 60 mg/dL) in patients with type 2 diabetes on multiple daily injections of insulin. Study subjects received NPH insulin (2-week run-in) followed by insulin glargine (8-week treatment phase). Glucose levels were measured by continuous glucose monitoring and self-monitored blood glucose profiles over the 72-hour pre- and post-treatment phase. Of 367 patients in the data set, 209 patients (56.9 %) experienced hypoglycemia according to continuous glucose monitoring; 97 (26.4 %) recorded hypoglycemia by conventional methods. Continuous glucose monitoring and self-monitoring of blood glucose reported similar mean daytime glucose levels at baseline and end point; however, nocturnal glucose levels were significantly lower with continuous glucose monitoring versus self-monitoring of blood glucose at baseline (130.2 versus 145.0 mg/dL) and at end point (123.3 versus 137.3 mg/dL).

The American Diabetes Association (2007) concluded that there is insufficient evidence to support the use of CGM in the hospital setting: "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 except in a research setting."

A major limitation of CGM is the durability and stability of the glucose sensors. Interstitial glucose concentrations, obtained with subcutaneous sensors, correlate with blood glucose concentrations. However, the sensors become progressively less accurate over time, so they can not be used on a maintenance basis, and must be changed every 3 days. Another potential concern is the 6 to 10 minutes delay in interstitial glucose sensor response to changes in serum glucose levels. This delay appears to be most important when glucose levels are falling rapidly, since it might result in development of clinically significant hypoglycemia before it was reflected in the sensor reading.

Artificial Pancreas or Bi-hormonal Bionic Endocrine Pancreas

An artificial pancreas is a closed-loop system with an insulin pump, real-time continuous glucose monitor and a small computing device to coordinate glucose sensing and insulin administration.

Closed-loop glucose management systems with a continuous glucose monitor and an insulin pump programmed with a computer algorithm that calculates insulin doses (or glucagon) from the CGM readings and tells the pump to deliver or temporarily suspend or reduce insulin based upon specified thresholds of measured glucose levels.

Aetna considers the Biostator System, a device which functions as an artificial pancreas, experimental and investigational. The Biostator is a glucose-controlled insulin infusion system developed in the early 1980's for use by a physician trained in the device. There are insufficient data in the published peer-reviewed medical literature documenting the safety and effectiveness of the Biostator. The Biostator is mainly used in research; it is rarely used in clinical practice.
Artificial Pancreas Device Systems with a Low Glucose Suspend Feature

Threshold suspend is the first step towards an artificial pancreas device system (APDS). This technology combines CGMS with an insulin pump which allows the user to set a low blood sugar threshold value. When the CGM sensor detects the preset low glucose threshold, insulin delivery is suspended. There is currently one FDA approved device of this type: the MiniMed 530G System.

The MiniMed 530G System is intended for continuous delivery of basal insulin (at user selectable rates) and administration of insulin boluses (in user selectable amounts) for the management of diabetes mellitus in persons, sixteen years of age and older, requiring insulin as well as for the continuous monitoring and trending of glucose levels in the fluid under the skin. This device automatically stops insulin delivery (for up to two hours) when sensor glucose values reach a preset level and when the individual does not respond to the threshold suspend alarm.

MiniMed Connect (compatible with MiniMed 530G with Enlite and MiniMed Paradigm Revel insulin pump) is an optional wireless device used to access continuous glucose monitor sensor data. Information can be viewed using an internet application through a smart device or via a browser accessible website and can be shared as needed.

A Blue Cross Blue Shield TEC Assessment was published in May, 2014 which evaluates the use of artificial pancreas device systems that include a low glucose suspend feature. The low glucose suspend feature uses a combination of an insulin pump, an continuous glucose monitor, a transmitter, and a computer algorithm to connect the insulin pump and continuous glucose monitor (e.g. the Medtronic MiniMed 530G System). In contrast to a continuous glucose monitor, a low glucose suspend feature does not require verification of the interstitial glucose level (e.g. by fingerstick), but rather sounds an alarm when the
continuous glucose monitor registers that glucose level has fallen to a predetermined level. If the alarm is not turned off, the device will suspend insulin delivery for up to 2 hours. The TEC Assessment based findings primarily on the in-home-arm of the ASPIRE trial, as they concluded that there is a dearth of comparative studies with a sample size of 15 or more subjects. The TEC Assessment concluded that further research is needed beyond the single ASPIRE study that met their criteria for inclusion in their assessment. Therefore, they concluded that the evidence is insufficient to permit conclusion on the impact of the artificial pancreas device system with low glucose suspend feature on health outcomes.

Bergenstal et al (2013) noted that the threshold-suspend feature of sensor-augmented insulin pumps is designed to minimize the risk of hypoglycemia by interrupting insulin delivery at a preset sensor glucose value. Therefore, the authors conducted a study in patients with nocturnal hypoglycemia to evaluate the efficacy and safety of sensor-augmented insulin-pump therapy with and without the threshold-suspend feature. Patients with type 1 diabetes and documented nocturnal hypoglycemia were randomly assigned to receive sensor-augmented insulin-pump therapy with or without the threshold-suspend feature for 3 months. Of a total of 247 patients, 127 patients were randomly assigned to receive sensor-augmented insulin-pump therapy with the threshold-suspend and 126 patients served as controls, receiving standard sensor-augmented insulin-pump therapy. The changes in glycated hemoglobin values were similar in the two groups with a mean AUC for nocturnal hypoglycemic events that was 37.5% lower in the threshold-suspend group than in the control group (980 ± 1200 mg per deciliter [54.4 ± 66.6 mmol per liter] × minutes vs. 1568 ± 1995 mg per deciliter [87.0 ± 110.7 mmol per liter] × minutes, P<0.001). Thus, hypoglycemic events occurred 31.8% less frequently in the threshold-suspend group than in the control group (1.5 ± 1.0 vs. 2.2 ± 1.3 per patient-week, P<0.001). During the study 1438 instances at night in which the pump was stopped for 2 hours were noted and the mean sensor glucose value was 92.6 ± 40.7 mg per
deciliter (5.1 ± 2.3 mmol per liter). Four control patients had a severe hypoglycemic event and no patients in either study group had diabetic ketoacidosis. The authors concluded that over a 3-month period the use of sensor-augmented insulin-pump therapy with the threshold-suspend feature reduced nocturnal hypoglycemia without increasing glycated hemoglobin values.

Additional studies supporting the conclusions drawn by Bergenstal et al (2013) are needed to support an evidence base for use of the artificial pancreas device system with a low-glucose suspense feature. It should be noted that Medtronic, Inc. received Premarket Approval for the MiniMed 530G System, which is a threshold suspend artificial pancreas device system, on September 26, 2013 (FDA, 2013).

**GlucoWatch Biographer**

Aetna considers the GlucoWatch Biographer (Cygnus Inc, Redwood City, CA.), a glucose meter that is worn on the wrist, experimental and investigational. The GlucoWatch Biographer provides non-invasive continuous glucose measurements, and is intended to detect trends in glucose levels in persons with diabetes. GlucoWatch measures the concentration of glucose by iontophoresis; a constant low-level electrical current is conducted through the skin, which causes glucose to be transported across the skin where it can be measured. After a 3-hr warm-up period and calibration from a fingerstick blood measurement, the device can provide up to 3 non-invasive glucose measurements per hour for up to 12 hours. Readings can be stored for several months and can be down-loaded into a computer. Clinical studies (Garg et al, 1999; Tamada et al, 1999) have reported correlations between GlucoWatch readings and standard fingerstick blood glucose measurements.

Because clinical studies showed that the GlucoWatch is less accurate than fingerstick testing, the device does not eliminate the need for painful fingersticks. In studies submitted to the FDA, measurements differed from fingerstick results by more
than 30 % up to 1/3 of the time. The GlucoWatch won't measure blood glucose levels if the person perspires excessively, and is less effective at detecting life-threatening low blood sugar than at spotting dangerously high glucose levels. According to the FDA-approved labeling, the GlucoWatch is intended to supplement, not replace, standard fingerstick testing. The product labeling states that users should never decide to use insulin based on a GlucoWatch measurement and that users should double-check the GlucoWatch reading with a fingerstick measurement before changing insulin dosages. In addition, the user must calibrate the GlucoWatch with a fingerstick reading each time the device is worn.

A structured evidence review conducted by the BlueCross BlueShield Association Technology Evaluation Center (TEC) (2002) concluded that the GlucoWatch Biographer does not meet the TEC criteria because the impact of this device on health outcomes is unknown.

A technology assessment conducted by CTAF concluded that the GlucoWatch Biographer does not meet CTAF's criteria (Tice, 2003). Furthermore, in a multi-center, randomized controlled study (n = 200), Chase et al (2005) concluded that use of the GlucoWatch G2 Biographer in addition to standard glucose monitoring did not improve glycemic control or reduce the frequency of severe hypoglycemia in children with type 1 diabetes.

Alternate Site Blood Glucose Monitors

Blood glucose monitors that permit "alternate site" testing allow persons to test blood samples obtained from sites other than their fingertips, such as the arm or thigh. The primary advantage of alternate site testing is that it may be less painful as there are fewer nerve endings at alternate sites than at the fingertips. However, people who draw blood frequently develop calluses which reduce the pain from fingerstick blood draws.
A Consumer Reports test of several alternate site meters concluded that alternate site testing is "slightly less painful" than fingertip testing. However, thigh samples were found to be "less convenient" than fingertip testing, and forearm samples were "harder to obtain and messier than finger pricks."

Although an alternative blood glucose monitor may be an appropriate choice for persons who can't use a conventional blood glucose monitor, there are a number of concerns about alternate site blood glucose monitors that argue against their routine prescription to all persons with diabetes. First, it is more difficult to start the bleeding at alternate sites, and it is more difficult to stop the bleeding once started. Blood draws from alternate sites may also induce bruising. Second, there is some concern about drawing blood from alternate sites because of diabetic persons' increased risk of infection. Risk of infection may be increased with alternate site testing because there is less blood flow at alternate sites than at fingertips.

A third concern is that alternate site testing may not reflect systemic glucose levels as accurately as finger-sticks, especially when blood glucose levels are rapidly changing, such as after a meal or exercise. This is because blood flow to alternate sites is slower than to the fingertips. Finally, there are no studies proving that alternate site testing improves compliance with blood glucose monitoring.

**Home Glycated Hemoglobin Monitors**

Aetna considers home glycated hemoglobin (HbA1c or A1C) monitors (e.g., A1cNow Diabetes Monitor, Metrika Inc., Sunnyvale, CA) experimental and investigational. There are no prospective clinical studies demonstrating improvements in compliance or other clinically significant benefits of home A1C testing over laboratory A1C testing. Because A1C testing reflects a mean glycemia over 2 to 3 months, the ADA recommends repeat A1C testing no more frequently than quarterly. Thus, A1C testing can be performed during regularly scheduled office visits. In addition, with office-based testing,
health care providers are available to properly interpret the test and to determine whether the person's treatment regimen needs to be modified. An assessment of home glycated hemoglobin monitors by the CTAF found that there is a paucity of data on home monitoring of HbA1c (Tice, 2003). One study (Rector et al, 2001) mailed free HbA1c kits to patients with diabetes reported that less than 50 % of the patients used the kits. The main reasons given for not performing the tests were that their physicians had already done the test or that they were too busy. The CTAF assessment (Tice, 2003) noted that "[d]ay to day clinical decisions about diabetes therapy are based on daily glucose testing, not HbA1c. HbA1c levels are usually used to make long-term changes in care in consultation between the patient and their doctor. It is unlikely that home HbA1c testing will improve clinical outcomes for patients with diabetes."

**Personal Digital Assistant-Based Blood Glucose Monitors**

Aetna considers a personal digital assistant-based blood glucose monitoring devices (e.g., TheraSense FreeStyle Tracker, Accu-Check Advantage Module) and module not medically necessary because they have not been shown in published clinical studies to improve clinical outcomes over standard blood glucose monitors. (Note: A personal digital assistant (PDA) does not meet Aetna's definition of covered DME in that the PDA can be used in the absence of illness or injury.)

The FreeStyle TrackerTM (TheraSense, Inc., Alameda, CA) and the Accu-Check Advantage Module (Roche Diagnostics Corp., Indianapolis, IN) combine a glucose meter with a PDA. Together, these create a glucose meter that also tracks and helps manage blood sugar (glucose) levels. Both the FreeStyle Tracker and the Accu-Check Advantage Module use a Handspring VisorTM PDA, which may be purchased separately. When a glucose module is inserted into its expansion slot, the PDA gives instructions for testing blood sugar and displays the results on its screen. The FreeStyle Tracker Diabetes Management System and the Accu-Check Advantage Module
were cleared by the FDA through 510(k) applications in June 2002.

To use these systems, an individual inserts a test strip into the glucose module, pierces the skin with a lancet, and places a drop of blood on the test strip. In addition to showing current blood sugar levels, these systems store readings in an electronic database. This database can also include insulin usage, food intake, exercise, and medicine. These data can be graphed and displayed on the PDA, or they can be uploaded to a personal computer (PC).

In addition, there is an unanswered question about whether these computerized tracking programs improve clinical outcomes. The ADA guidelines (2003) concluded: "Although a number of SMBG [self-monitoring of blood glucose] methods store test results and with a computer interface can provide sophisticated analyses of blood glucose data, it is not known whether use of these data management systems yields better glucose control than patient review of results recorded in a logbook."

There is no published clinical literature demonstrating that proves that the use of PDA-based blood glucose monitors improves clinical outcomes over standard blood glucose monitors.

Sevick et al. (2008) noted that ENHANCE is a randomized controlled trial to test an intervention designed to improve regimen adherence in adults with type 2 diabetes. The intervention, based on Social Cognitive Theory (SCT), is paired with PDA-based self-monitoring. The authors described the: (i) manner in which PDA-based self-monitoring is integrated within the SCT-based intervention, (ii) feasibility and acceptability of PDA-based dietary self-monitoring, and (iii) issues encountered in teaching participants to self-monitor using a PDA. During the first 30 months of this 5-year study, 232 subjects were screened and 151 were randomized. A total of 6 cohorts completed the study. The retention rate is 85 % (n = 129). Of those
randomized to the intervention \( n = 74 \) and completing the study \( n = 61 \), 88 \% reported understanding the usefulness of PDA-monitoring, 85 \% reported ease in entering foods into the device, 70 \% reported ease in interpreting feedback graphs, and 82 \% indicated that they would continue to use the PDA for self-monitoring after the study concluded. Assuming 3 meals per day, subjects entered an average of 58 \% of their meals in their PDA, and 43 \% were entered assuming 4 meals per day. If the investigators eliminated from the analysis those individuals who entered less than 10 \% of their expected meals \( n = 12 \), the average rate of self-monitoring was 69 \% assuming 3 meals per day, and 52 \% assuming 4 meals per day. The authors concluded that PDA-based dietary monitoring is perceived by participants to be useful and acceptable, and PDA technology shows promise as a tool for assisting those with type 2 diabetes in their efforts to manage their disease.

\textit{Disposable Blood Glucose Monitors}

Aetna considers a disposable blood glucose monitor (e.g., the ReliOn NewTek (Hypoguard USA, Inc., Edina, MN)) an acceptable medically necessary alternative to a standard blood glucose monitor. The ReliOn NewTek has been cleared by the FDA for marketing under the 510(k) process for persons with diabetes when recommended by their physician. It includes a disposable meter containing 100 test strips plus control solution. The ReliOn NewTek (Express Blood Glucose Monitoring System) received FDA 510(k) marketing clearance in 2003. According to the FDA 510(k) summary letter submitted by the manufacturer to the FDA, testing demonstrated that its performance was substantially equivalent to the Hypoguard Advance Blood Glucose Monitoring System.

\textit{Infrared Thermometer Device}

Foot ulcers develop in approximately 15 \% of patients with diabetes. Ulceration is caused by several factors, but particularly by neuropathy. The annual incidence of foot ulceration is slightly more than 2 \% among all patients with
diabetes and between 5 and 7.5 % among diabetic patients with peripheral neuropathy. Peripheral neuropathy results in loss of the protective sensation of pain and in autonomic dysfunction, with sympathetic denervation, dry skin, and warm feet. Appropriate medical education regarding early assessment for lesions or warning signs of imminent ulceration in patients with sensory loss is essential. Other causes of ulceration include peripheral vascular disease, callus, edema, and deformity. The triad of neuropathy, deformity, and trauma is present in almost two-thirds of patients with foot ulcers. Inappropriate footwear is the most common source of trauma.

Neuropathy can be detected with a simple neurological examination of the lower extremities involving the use of a 10-g monofilament to test sensation, or a composite score such as the modified neuropathy disability score. Both are predictive of the risk of foot ulcers. The modified neuropathy disability score assigns a number to each of the following: (i) vibration threshold utilizing a tuning fork, (ii) temperature (tuning fork placed in ice water or warm water), (iii) pinprick, and (iv) Achilles' reflex. A score of 6 or greater is predictive of foot ulceration.

The TempTouch (Diabetica Solutions Inc., San Antonio, TX) is an infrared hand-held, battery-operated thermometer intended for the intermittent measurement and monitoring of human skin surface temperature. It received 510(k) marketing clearance from the FDA in March, 2005 and is being marketed as an early warning device for the development of diabetic foot neuropathy. Individuals take temperatures on the bottom of both feet with the device and compare results from one day to the next. If there is a 4-degree Fahrenheit difference on the same spot (e.g., the heel of one foot versus the other) from one day to the next, the spot with the higher temperature is a 'hot spot' and may be predictive of an ulceration.

Lavery and colleagues (2004) evaluated the effectiveness of at-home infrared temperature monitoring as a preventative tool in individuals at high risk for diabetes-related lower-extremity
ulceration and amputation in 85 patients who fit diabetic foot risk category 2 or 3 (neuropathy and foot deformity or previous history of ulceration or partial foot amputation). Patients were randomized into a standard therapy group (n = 41) or an enhanced therapy group (n = 44). Standard therapy consisted of therapeutic footwear, diabetic foot education, and regular foot evaluation by a podiatrist. Enhanced therapy included the addition of a handheld infrared skin thermometer to measure temperatures on the sole of the foot in the morning and evening. Elevated temperatures (greater than 4 degrees Fahrenheit compared with the opposite foot) were considered to be "at risk" of ulceration due to inflammation at the site of measurement. When foot temperatures were elevated, subjects were instructed to reduce their activity and contact the study nurse. Study subjects were followed for 6 months and included a podiatry evaluation every 10 to 12 weeks. The enhanced therapy group had significantly fewer diabetic foot complications (enhanced therapy group 2% versus standard therapy group 20%, p = 0.01, odds ratio 10.3, 95% CI: 1.2 to 85.3). There were 7 ulcers and 2 Charcot fractures among standard therapy patients and one ulcer in the enhanced therapy group. The authors concluded that these results suggest that at-home patient self-monitoring with daily foot temperatures may be an effective adjunctive tool to prevent foot complications in individuals at high-risk for lower-extremity ulceration and amputation. However, Parrella et al (2005) reviewed the study by Lavery and colleagues (2004) and stated, "Although these results suggest effectiveness, they may be influenced by patients changing activity levels in the TemPTouch and/or seeking a clinical evaluation by the study nurse when temperature differences were noted."

Lavery and colleagues (2007) conducted a further study with a follow-up period of 15 months. Diabetics with a previous history of diabetic foot ulceration (n = 173) were assigned to standard therapy, structured foot examination, or enhanced therapy groups. Each group received therapeutic footwear, diabetic foot education, and regular foot care. Subjects in the structured foot examination group performed a structured foot
inspection daily and recorded their findings in a logbook. If standard therapy or structured foot examinations identified any foot abnormalities, subjects were instructed to contact the study nurse immediately. Subjects in the enhanced therapy group used an infrared skin thermometer to measure temperatures on 6 foot sites each day. Temperature differences greater than 4 degrees Fahrenheit (greater than 2.2 degrees Celsius) between left and right corresponding sites triggered patients to contact the study nurse and reduce activity until temperatures normalized. The enhanced therapy group had fewer foot ulcers than the standard therapy and structured foot examination groups (enhanced therapy 8.5 versus standard therapy 29.3 %, p = 0.0046 and enhanced therapy versus structured foot examination 30.4 %, p = 0.0029). Patients in the standard therapy and structured foot examination groups were 4.37 and 4.71 times more likely to develop ulcers than patients in the enhanced therapy group. The authors concluded that infrared temperature home monitoring, in serving as an "early warning sign," appears to be a simple and useful adjunct in the prevention of diabetic foot ulcerations.

Armstrong and colleagues (2007) evaluated the effectiveness of home temperature monitoring and the incidence of foot ulcers in high-risk patients with diabetes. Diabetics at high risk for ulceration (n = 225) were randomly assigned to standard therapy (standard therapy group) or dermal thermometry (dermal thermometry group) groups. Both groups received therapeutic footwear, diabetic foot education, regular foot care, and performed a structured foot inspection daily. The dermal thermometry group used an infrared skin thermometer to measure temperatures on 6 foot sites twice daily. Temperature differences greater than 4 degrees Fahrenheit between left and right corresponding sites triggered patients to contact the study nurse and reduce activity until temperatures normalized. A total of 8.4 % (n = 19) subjects ulcerated over the 18-month study period. Subjects were 1/3 as likely to ulcerate in the dermal thermometry group compared with the standard therapy group (12.2 % versus 4.7 %, odds ratio 3.0, 95 % CI: 1.0 to 8.5, p = 0.038). Proportional hazards regression analysis
suggested that thermometry intervention was associated with a significantly longer time to ulceration ($p = 0.04$), adjusted for elevated foot ulcer classification (International Working Group Risk Factor 3), age, and minority status. Patients that ulcerated had a temperature difference that was 4.8 times greater at the site of ulceration in the week before ulceration than did a random 7 consecutive-day sample of 50 other subjects that did not ulcerate ($3.50 +/- 1.0$ versus $0.74 +/- 0.05$, $p = 0.001$). The authors concluded that high temperature gradients between feet may predict the onset of neuropathic ulceration and self-monitoring may reduce the risk of ulceration.

In a clinical pilot study, Fierheller and Sibbald (2010) quantified the relationship between increased peri-wound skin temperature and wound infection, as well as validated use of a hand-held infrared thermometer for the wound care practitioner. Using a cross-sectional design, 2 groups of participants were recruited from a chronic wound clinic: (i) without wounds ($n = 20$) and (ii) with chronic leg ulcers ($n = 40$). Participants and wound characteristics were documented. All skin temperatures were documented using a hand-held infrared thermometer under consistent environmental conditions within the clinic. Data analysis was based on the difference (Delta) in skin temperature (in degrees Fahrenheit) between a target or wound site and an equivalent contralateral control site. Wound infection was identified using the combination of a validated assessment tool and clinical judgment. Supplemental semi-quantitative bacterial swabs were collected from all wounds. Descriptive statistics were analyzed using the chi-squared calculation. A Pearson $r$ calculation of test-retest skin temperature data collected from non-wounded participants initially determined reliability of the infrared thermometer. Correlation of increased peri-wound skin temperature to wound infection was determined by calculation of a 1-way analysis of variance. The infrared thermometer was found to be reliable ($r = 0.939$, $p = 0.000$ at a 95 % CI). A statistically significant relationship between increased peri-wound skin temperature and wound infection was identified ($F = 44.238$, $p = 0.000$ at a 95 % CI). Neither
patient nor wound characteristics were significantly different between the participants with non-infected or infected wounds. The authors concluded that these findings demonstrated that incorporating quantitative skin temperature measurement into routine wound assessment provides a timely and reliable method for a wound care practitioner to quantify the heat associated with deep and surrounding skin infection and to monitor ongoing wound status. Study limitations may reduce transferability of these findings to wound types other than chronic leg ulcers. They stated that further research is needed to support and strengthen these results.

The International Working Group on the Diabetic Foot practice guidelines (1999) recommended that all individuals with diabetes be examined at least annually for potential foot problems and that the risk of future ulceration can be determined with a 10-g monofilament to test sensation. These guidelines are supported in part by data from clinical trials and in part by expert opinion.

The American College of Foot and Ankle Surgeons clinical practice guideline on diabetic foot disorders (2006) outlined a preventive treatment strategy for the diabetic foot and stated that home temperature assessment of the foot has been shown to reduce the incidence of foot ulcers 10-fold compared with standard preventive care (citing the 2004 study by Lavery and colleagues).

The ADA’s clinical practice recommendations on preventive foot care for diabetics recommends a foot examination at least annually by a health care provider and patient education regarding preventive foot care (ADA, 2010).

There is insufficient evidence of the effectiveness of an infrared thermometer device versus standard foot care in reducing the risk for diabetic foot ulceration.

*Measurement of Advanced Glycation End Products by Skin Autoflourescence*
Skin autofluorescence is a non-invasive measurement of the level of tissue accumulation of advanced glycation end products (AGEs), representing cumulative glycemic and oxidative stress. Several studies have shown that AGEs accumulate in skin faster in individuals with poor blood sugar control and that measurement of AGEs by skin autofluorescence may be able to predict the risk of developing diabetes and related complications (Lutgers et al, 2006 and 2009; Meerwald et al, 2007; Gerrits et al, 2008; and Ediger et al, 2009).

The Scout DS system (Veralight, Inc., Albuquerque, NM) measures skin AGEs by autoflorescence spectroscopy. The device is a portable desktop system with an arm cradle. The subject places the palm side of their forearm into the cradle and the device shines multiple wavelengths of light into the skin causing the AGEs to fluoresce. The instrument optically calibrates for skin pigmentation, making the measurement impervious to variations in skin color. A specially designed fiber-optic probe sends excitation light to the subject and relays resulting skin fluorescence to the detection module. A value from 0 to 100 representing the likelihood of that subject having an abnormal glucose tolerance test is reported in about 60 seconds. The proposed benefits of the Scout DS system is that the patient would not need to fast or provide a blood sample and results are received much quicker. The system is not intended to replace an oral glucose tolerance test.

There is insufficient evidence of the effectiveness of the Scout DS system compared to fasting plasma glucose tolerance testing. The device is currently used for research purposes only. The manufacturer is conducting a prospective, multi-center clinical trial comparing the Scout DS system to the fasting plasma glucose tolerance test in subjects at risk for diabetes.

de Ranitz-Greven et al (2012) noted that AGEs are tissue proteins that accumulate with age and in DM. Advanced glycation end products can be measured by the AGE-Reader (DiagnOptics Technologies BV, Groningen, The Netherlands),
which measures skin auto-fluorescence (SAF); SAF has been suggested as a measure to screen for undiagnosed DM or impaired glucose tolerance. Skin auto-fluorescence has never been investigated in GDM. Therefore, these researchers compared SAF at diagnosis in GDM patients with normal pregnancy. If SAF is elevated in GDM, future research could focus on the possible use of the AGE-Reader as a screening method for GDM. In this mono-center observational study, SAF was measured in 60 GDM patients at diagnosis and 44 pregnant women without diabetes. Skin auto-fluorescence did not differ between GDM at diagnosis (mean [SD], 1.74 [0.31] arbitrary units) and normal pregnancy (1.76 [0.32] arbitrary units); SAF was lower in white European patients than in patients with other ethnicity. The authors concluded that this first study of tissue AGE accumulation in pregnancy shows no differences in SAF between women with GDM at diagnosis and normal pregnancy. This was most likely due to mild severity and short duration of hyperglycemia in GDM at diagnosis, but it did not exclude potential differences in SAF later in pregnancy. However, the fact that no differences were detected at diagnosis made it unlikely that the AGE-Reader can be developed as a screening method for GDM in the future. Furthermore, these investigators found that ethnicity should be taken into account when measuring SAF.

Temma et al (2015) stated that AGEs are thought to play a major role in the pathogenesis of diabetic vascular complications. Skin autofluorescence was recently reported to represent tissue AGEs accumulation with a non-invasive method. These researchers evaluated association between AF value and diabetic vascular complications (e.g., retinopathy, nephropathy and cervical atherosclerosis) using the carotid intima-media thickness (IMT), an established marker of cardiovascular disease in patients with type 2 diabetes. A total of 68 patients with type 2 diabetes were enrolled in a cross-sectional manner; AGEs accumulation was measured with AF reader. Clinical parameters were collected at the time of AF and IMT measurement. Max-IMT was correlated with age and AF ($r = 0.407$, $p = 0.001$), but not with HbA1c, GA, and
pentosidine. Also, AF was not correlated with HbA1c, GA and pentosidine, but was correlated with age (r = 0.560, p < 0.001), duration of diabetes (r = 0.256, p < 0.05). Multivariate regression analysis revealed that AF, but not age, was an independent determinant of max-IMT. The authors concluded that AF might be a beneficial surrogate marker for evaluating carotid atherosclerosis in patients with type 2 diabetes non-invasively.

Yamagishi et al (2015) noted that a non-enzymatic reaction between reducing sugars and the amino groups of proteins, lipids and nucleic acids is known as the "Maillard reaction". The reactions have progressed in a normal aging process and at an accelerated rate under hyperglycemic, inflammatory, and/or oxidative stress conditions, thus leading to the formation and accumulation of AGEs. Cross-linking modification of organic matrix proteins such as collagen by AGEs not only leads to an increase in vascular and myocardial stiffness, but also deteriorates structural integrity and physiological function of multiple organ systems. Furthermore, there is a growing body of evidence that interaction of AGEs with a cell surface receptor RAGE elicits oxidative stress generation and subsequently evokes inflammatory, thrombogenic and fibrotic reactions, thereby being involved in the development and progression of various age- or diabetes-related disorders, including cardiovascular disease (CVD), Alzheimer's disease, osteoporosis, cancer growth and metastasis. Skin AGE levels measured in biopsy specimens are associated with the development and progression of diabetic microangiopathy. Recently, accumulation levels of AGEs in the skin can be measured non-invasively by autofluorescence. The authors concluded that accumulating evidence has suggested that SAF is correlated with the presence and severity of vascular complications of diabetes and could predict future cardiovascular events and death in patients with diabetes.

Post-Partum Screening for Diabetes

testing in a cohort of women with gestational diabetes mellitus (GDM). A validated computerized algorithm using Kaiser Permanente Northwest automated data systems identified 36,251 live‐births or still‐births from 1999 through 2006. The annual percentage of pregnancies complicated by GDM with clinician orders for and completion of a fasting plasma glucose (FPG) test within 3 months of delivery was calculated. Logistic regression with generalized estimating equations was used to test for statistically significant trends. The percentages of pregnancies affected by GDM increased from 2.9 % in 1999 to 3.6 % in 2006 (p < 0.01). Clinician orders for post‐partum tests increased from 15.9 % in 1999 to 79.3 % in 2004 (p < 0.01), and then remained stable through 2006. Completed FPG tests increased from 9.0 % in 1999 to 57.8 % in 2004 (p < 0.01), and then remained stable through 2006. No oral glucose tolerance tests were ordered. From 2004 to 2006, the practice site where women received care was the factor most strongly associated with the clinician order, but it was not predictive of test completion. Among women with clinician orders, those who were Asian or Hispanic or who attended the 6‐week post‐partum examination were more likely to complete the test than their counterparts. The authors concluded that post‐partum glucose testing in women with GDM‐affected pregnancies increased over time. However, even in recent years, 42 % of women with GDM‐affected pregnancies failed to have a post‐partum FPG test, and no test was ordered for 21 % of GDM‐affected pregnancies.

The American College of Obstetricians and Gynecologists' Committee opinion on post‐partum screening for abnormal glucose tolerance in women who had GDM (ACOG 2009) stated that establishing the diagnosis of GDM offers an opportunity not only to improve pregnancy outcome, but also to decrease risk factors associated with the subsequent development of type 2 diabetes. The ACOG's Committee on Obstetric Practice recommends that all women with GDM be screened at 6 to 12 weeks post‐partum and managed appropriately.

*Continuous Glucose Monitoring Following Gastric Bypass and*
Hanaire et al. (2010) stated that hypoglycemia is rare after a gastric bypass and can be taken for a dumping syndrome. There is no report in the literature of the contribution of continuous glucose monitoring (CGM) to the diagnosis of hypoglycemia in these circumstances. The present case report showed that CGM can be a useful tool for the diagnosis and the management of such episodes. Continuous glucose monitoring revealed hypoglycemic episodes in free living circumstances that were not present during 72-hr fasting. These episodes followed wide hyperglycemic swings. No such episode resumed over 8 months after specific dietary advices and treatment by 50 mg TID of acarbose. Because hypoglycemia can be difficult to diagnose from dumping syndrome, CGM is a very useful tool revealing the episodes in free-living circumstances and can be used to monitor the treatment success. The findings of this single-case study need to be validated by well-designed studies.

Hanaire et al. (2011) evaluated glucose variability after gastric bypass CGM in a real-life setting. Continuous glucose monitoring was performed for 4.2 +/- 1.3 days in 3 groups of 10 subjects each: (i) patients who had undergone gastric bypass and who were referred for post-prandial symptoms compatible with mild hypoglycemia, (ii) non-operated diabetes controls, and (iii) healthy controls. The maximum interstitial glucose (IG), SD of IG values, and mean amplitude of glucose excursions (MAGE) were significantly higher in operated patients and in diabetes controls than in healthy controls. The time to the post-prandial peak IG was significantly shorter in operated patients (42.8 +/- 6.0 mins) than in diabetes controls (82.2 +/- 11.1 mins, p = 0.0002), as were the rates of glucose increase to the peak (2.4 +/- 1.6 versus 1.2 +/- 0.3 mg/ml/min; p = 0.041). True hypoglycemia (glucose less than 60 mg/dL) was rare: the symptoms were probably more related to the speed of IG decrease than to the glucose level achieved. Half of the operated patients, mostly those with a diabetes background before surgery, had post-prandial glucose concentrations above 200 mg/dL (maximum IG, 306 +/- 59 mg/dL), in contrast to the
normal glucose concentrations in the fasting state and 2 hrs post-meal. The authors concluded that glucose variability is exaggerated after gastric bypass, combining unusually high and early hyperglycemic peaks and rapid IG decreases. This might account for post-prandial symptoms mimicking hypoglycemia but often seen without true hypoglycemia. Early post-prandial hyperglycemia might be under-estimated if glucose measurements are done 2 hrs post-meal. This study reported on differences in glycemia in persons with diabetes who had undergone obesity surgery, persons with diabetes without obesity surgery, and normal controls. It did not report on the use of the CGM in clinical management.

UpToDate reviews on "Medical management of patients after bariatric surgery" (Kushner and Cummings, 2012) and "Complications of bariatric surgery" (Adair and Ellsmere, 2012) do not mention the use of continuous glucose monitoring.

There is a lack of published studies on the use of continuous glucose monitors in nesidioblastosis. An UpToDate review on “Pathogenesis, clinical features, and diagnosis of persistent hyperinsulinemic hypoglycemia of infancy” (Sunehag and Haymond, 2013) states that “Persistent hyperinsulinemic hypoglycemia of infancy (PHHI), also referred to as congenital hyperinsulinism, familial hyperinsulinemic hypoglycemia, and primary islet cell hypertrophy (nesidioblastosis), is the most common cause of persistent hypoglycemia in neonates and infants. PHHI is a genetic disorder with both familial and sporadic forms, characterized by dysregulation of insulin secretion. Early recognition, diagnosis, and treatment are necessary to prevent or minimize neurologic damage from recurrent or prolonged episodes of hypoglycemia”. However, this review does not mention the use of continuous glucose monitoring as a management tool.

**Glucose Meters for Persons with Visual Impairment**

There are blood glucose monitoring systems designed especially for use by those with visual impairments. The
monitors used in such systems are identical in terms of reliability and sensitivity to standard blood glucose monitors. They differ by having such features as voice synthesizers, automatic timers, and specially designed arrangements of supplies and materials to enable the visually impaired to use the equipment without assistance.

**Mobile Application Software for Self-Management of Diabetes**

The effectiveness of mobile phone applications in improving diabetes outcomes has not been established (Mendoza & Rosenberg, 2013). In a systematic review of 22 trials evaluating mobile phone interventions for self-management (eg, text messaging, phone reminders, and coaching interventions), investigators observed a modest (0.5%) decrease in HbA1c levels over a median followup period of 6 months (Liang, et al., 2011). Studies examining the long-term benefit of mobile phone applications in improving clinical outcomes in diabetes are necessary (Mendoza & Rosenberg, 2013).

**Hypoglycemic Wristband Alarm (e.g., Sleep Sentry)**

Hypoglycemic alarms are skin temperature/skin conductance devices for detecting nocturnal hypoglycemia. Through sensors on the back surface of the device, electronic information is sent to a built-in microprocessor. When there is deviation from preset levels for skin temperature and/or perspiration, an alarm will sound. The device may be worn on the ankle, forearm, or wrist. One of the disadvantages of these devices for alerting hypoglycemia is that activities that cause changes in skin temperature and/or perspiration can set off false alarms. An example of this device is the Sleep Sentry. However, the clinical utility of these devices has not been proven.

Hansen and Duck (1983) examined the effectiveness of the Teledyne Sleep Sentry in detecting nocturnal hypoglycemia in pediatric patients. A total of 24 insulin-dependent diabetic pediatric subjects were studied for 1,444 nights for detection of nocturnal hypoglycemia with the Teledyne Sleep Sentry: a
wristwatch-like unit that measures absolute changes in skin temperature and decreases in galvanic skin resistance, indicators of hypoglycemia. The device detected 42 of 46 recognized hypoglycemic episodes; 150 alarms were sounded without evidence of hypoglycemia, probably due to night sweating; 25% of the subjects experienced unacceptable cutaneous reactions, presumably due to metallic iontophoresis.

Johansen and colleagues (1986) examined the effectiveness and credibility of a skin temperature/skin conductance meter (Teledyne Sleep Sentry) for detecting hypoglycemia during night-time in 22 adult insulin-treated diabetics. Capillary blood glucose concentration was measured 99 times (when the alarm sounded, in case of hypoglycemic symptoms, and at 3 a.m.). Hypoglycemia was defined as a capillary blood glucose concentration of less than or equal to 3 mmol/L. Blood glucose was measured 61 times in connection with sounding of the alarm and 38 times without the alarm sounding. At 3 a.m. the Sleep Sentry sounded the alarm 22 times, of which hypoglycemia was present 6 times giving a diagnostic specificity or diagnostic true positive rate of 0.27 (95% CI: 0.11 to 0.50). In 35 of 38 cases of no alarm the blood glucose was greater than 3 mmol/L, giving a diagnostic sensitivity of 0.92 (95% CI: 0.79 to 0.98). The Sleep Sentry sounded the alarm in 6 of 9 cases of hypoglycemia, giving a nosological sensitivity of 0.67 (95% CI: 0.30 to 0.93). The Sleep Sentry did not sound the alarm in 35 of 51 cases of non-hypoglycemia, giving a nosological specificity of 0.69 (95% CI: 0.54 to 0.81). The authors concluded that the Sleep Sentry detected about 2/3 of blood glucose values less than or equal to 3 mmol/L, but in addition it sounded a false alarm in 2/3 of the cases.

Clarke et al (1988) reported metabolic and cutaneous events associated with hypoglycemia detected by the Sleep Sentry. A total of 18 insulin-dependent diabetic subjects [age (mean +/- SD) 33.2 +/- 10.6 years] participated in a study designed to determine the metabolic and cutaneous parameters associated with activation of the nocturnal hypoglycemia monitor Sleep Sentry. Plasma glucose, glucagon, epinephrine,
norepinephrine, and pancreatic polypeptide concentrations were determined every 10 minutes during a 2-hour constant intravenous insulin infusion (40 mU/kg/hour). In addition, skin temperature and electrical conductance were monitored at the same time intervals, and subjects were asked to rate the degree to which they felt cold and/or sweaty. Ten of the subjects (alarmers) activated the device with a mean plasma glucose nadir of 52.8 +/- 13.8 mg/dL, whereas 8 (non-alarmers) failed to do so despite a mean plasma glucose nadir of 50.5 +/- 8.2 mg/dL. There were no significant differences between alarmers and non-alarmers with respect to initial or nadir plasma glucose levels, rate of fall of plasma glucose, or changes in plasma epinephrine, norepinephrine, or pancreatic polypeptide concentrations. In addition, changes in skin temperature and conductance were similar in both groups as were descriptive variables including age, disease duration, gender, and level of glucose control. No subject reported an increase in coldness, whereas 80% of both groups reported an increase in sweatiness; 3 subjects studied on more than one occasion over a year failed to exhibit consistent activation of the alarm. The authors concluded that the findings of this study suggested that it may not be possible to identify patients for whom the Sleep Sentry would be a reliable addition to their self-management regimen and that physicians should exercise caution in recommending its use.

Remote Glucose Monitoring (e.g., the Dexcom SHARE)

On October 20, 2014, Dexcom, Inc. (San Diego, CA) announced that it has received FDA approval for its CGM remote mobile communications device: Dexcom SHARE, which is an accessory to the Dexcom G4® PLATINUM Continuous Glucose Monitoring System. It uses a secure wireless connection to transmit the glucose levels of a person with diabetes to the smartphones of up to 5 designated recipients, or “followers”. These followers can remotely monitor a patient’s glucose information and receive alert notifications from almost anywhere via their Apple® iPhone® or iPod® touch. With Dexcom SHARE, parents and personal caregivers can monitor a child’s or loved one’s
glucose data from a remote location.


- The Dexcom SHARE consists of a small cradle device in which the Dexcom G4 PLATINUM is docked. The cradle also functions as a battery charger for the receiver and must be connected to an electrical outlet.
- The Dexcom SHARE cradle is equipped with Bluetooth technology, enabling the device to wirelessly transmit glucose levels from the Dexcom G4 PLATINUM receiver to the Dexcom SHARE App on the patient’s Apple® iPhone® or iPod® touch.
- The Dexcom SHARE App uploads glucose data to a secure server. Personal caregivers or parents can then remotely receive notifications about glucose levels and trends on their Apple® iPhone® or iPod® touch.

However, there is a lack of evidence that the Dexcom SHARE would improve health outcomes of patients with diabetes.

In a systematic review, Mushcab et al (2015) evaluated evidence for viability and impact of Web-based tele-monitoring for managing type 2 diabetes mellitus. A review protocol included searching Medline, EMBASE, CINAHL, AMED, the Cochrane Library, and PubMed using the following terms: telemetry, type 2 diabetes mellitus, self-management, and web-based Internet solutions. The technology used, trial design, quality of life measures, and the HbA1c levels were extracted. This review identified 426 publications; of these, 19 met preset inclusion criteria. Ten quasi-experimental research designs were found, of which 7 were pre-posttest studies, 2 were cohort studies, and 1 was an interrupted time-series study; in addition, there were nine randomized controlled trials (RCTs). Web-based remote monitoring from home to hospital is a viable approach for healthcare delivery and enhances
patients' quality of life. Six of these studies were conducted in South Korea, 5 in the United States, 3 in the United Kingdom, 2 in Taiwan, and 1 each in Spain, Poland, and India. The duration of the studies varied from 4 weeks to 18 months, and the participants were all adults. Fifteen studies showed positive improvement in HbA1c levels; 1 study showed high acceptance of the technology among participants. The authors concluded that it remains challenging to identify clear evidence of effectiveness in the rapidly changing area of remote monitoring in diabetes care. They stated that both the technology and its implementations are complex; the optimal design of a telemedicine system is still uncertain, and the value of the real-time blood glucose transmissions is still controversial.

Karhula and colleagues (2015) examined if a structured mobile phone-based health coaching program, which was supported by a remote monitoring system, could be used to improve the health-related quality of life (HRQL) and/or the clinical measures of type 2 diabetes and heart disease patients. A randomized controlled trial was conducted among type 2 diabetes patients and heart disease patients of the South Karelia Social and Health Care District. Patients were recruited by sending invitations to randomly selected patients using the electronic health records system. Health coaches called patients every 4 to 6 weeks and patients were encouraged to self-monitor their weight, blood pressure, blood glucose (diabetics), and steps (heart disease patients) once per week. The primary outcome was HRQL measured by the Short Form (36) Health Survey (SF-36) and HbA1c among diabetic patients. The clinical measures assessed were blood pressure, weight, waist circumference, and lipid levels. A total of 267 heart patients and 250 diabetes patients started in the trial, of which 246 and 225 patients concluded the end-point assessments, respectively. Withdrawal from the study was associated with the patients' unfamiliarity with mobile phones -- of the 41 drop-outs, 85 % (11/13) of the heart disease patients and 88 % (14/16) of the diabetes patients were familiar with mobile phones, whereas the corresponding percentages were 97.1 % (231/238) and 98.6 % (208/211), respectively, among the rest
of the patients (p = 0.02 and p = 0.004). Withdrawal was also associated with heart disease patients' co-morbidities – 40 % (8/20) of the drop-outs had at least 1 comorbidity, whereas the corresponding percentage was 18.9 % (47/249) among the rest of the patients (p = 0.02). The intervention showed no statistically significant benefits over the current practice with regard to HRQL — heart disease patients: beta = 0.730 (p = 0.36) for the physical component score and beta = -0.608 (p = 0.62) for the mental component score; diabetes patients: beta = 0.875 (p = 0.85) for the physical component score and beta = -0.770 (p = 0.52) for the mental component score. There was a significant difference in waist circumference in the type 2 diabetes group (beta = -1.711, p = 0.01). There were no differences in any other outcome variables. The authors concluded that a health coaching program supported with tele-monitoring did not improve heart disease patients' or diabetes patients' quality of life or their clinical condition. There were indications that the intervention had a differential effect on heart patients and diabetes patients. Diabetes patients may be more prone to benefit from this kind of intervention. This should not be neglected when developing new ways for self-management of chronic diseases.

Furthermore, an UpToDate review on “Blood glucose self-monitoring in management of adults with diabetes mellitus” (Mcculloch, 2015) does not mention remote glucose monitoring as a management tool.

**Appendix**

**Medically Necessary Quantities of Diabetic Supplies (Test Strips, Lancets)**

**Usual Utilization**

- For members with diabetes who are not currently being treated with insulin injections, up to 100 test strips and up to 100 lancets every 3 months are considered medically necessary.
For members with diabetes who are currently being treated with insulin injections, up to 300 test strips and up to 300 lancets every 3 months are considered medically necessary.

High Utilization

For members with diabetes who are not currently being treated with insulin injections, more than 100 test strips and more than 100 lancets every 3 months are considered medically necessary if criteria (a) – (c) below are met.

For members with diabetes who are currently being treated with insulin injections, more than 300 test strips and more than 300 lancets every 3 months are considered medically necessary if criteria (a) – (c) below are met.

a. The member’s physician has concluded that the member (or the member’s caregiver) has sufficient training using the particular device prescribed as evidenced by providing a prescription for the appropriate supplies and frequency of blood glucose testing; and

b. The treating physician has seen the member, evaluated their diabetes control within 6 months prior to ordering quantities of strips and lancets that exceed the utilization guidelines and has documented in the member’s medical record the specific reason for the additional materials for that particular member; and

c. If refills of quantities of supplies that exceed the utilization guidelines are dispensed, there must be documentation in the physician's records (e.g., a specific narrative statement that adequately documents the frequency at which the member is actually testing or a copy of the member’s log) that the member is actually testing at a frequency that corroborates the quantity of supplies that have been dispensed. If the member is regularly using quantities of supplies that exceed the utilization guidelines, new documentation must be present at least every six months.
**CPT Codes / HCPCS Codes / ICD-10 Codes**

*Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":*

**CPT codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0403T</td>
<td>Preventive behavior change, intensive program of prevention of diabetes using a standardized diabetes prevention program curriculum, provided to individuals in a group setting, minimum 60 minutes, per day</td>
</tr>
<tr>
<td>82947</td>
<td>Glucose; quantitative, blood (except reagent strip)</td>
</tr>
<tr>
<td>82948</td>
<td>blood, reagent strip</td>
</tr>
<tr>
<td>82950</td>
<td>post glucose dose (includes glucose)</td>
</tr>
<tr>
<td>82962</td>
<td>Glucose, blood by glucose monitoring device(s) cleared by the FDA specifically for home use</td>
</tr>
<tr>
<td>83519</td>
<td>Immunoassay, analyte, quantitative; by radiopharmaceutical technique (eg, RIA)</td>
</tr>
<tr>
<td>86341</td>
<td>Islet cell antibody</td>
</tr>
</tbody>
</table>

**CPT codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81506</td>
<td>Endocrinology (type 2 diabetes), biochemical assays of seven analytes (glucose, HbA1c, insulin, hs-CRP, adiponectin, ferritin, interleukin 2-receptor alpha), utilizing serum or plasma, algorithm reporting a risk score [PreDx Diabetes Risk Score]</td>
</tr>
</tbody>
</table>

**Other CPT codes related to the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>83036</td>
<td>Hemoglobin; glycosylated (A1C)</td>
</tr>
<tr>
<td>83037</td>
<td>glycosylated (A1C) by device cleared by FDA for home use</td>
</tr>
<tr>
<td>97802</td>
<td>Medical nutrition therapy; initial assessment and intervention, individual, face-to-face with the patient, each 15 minutes</td>
</tr>
<tr>
<td>97803</td>
<td>re-assessment and intervention, individual, face-to-face with the patient, each 15 minutes</td>
</tr>
<tr>
<td>97804</td>
<td>group (2 or more individual(s)), each 30 minutes</td>
</tr>
</tbody>
</table>
**HCPCS codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A4206</td>
<td>Syringe with needle, sterile 1 cc or less, each</td>
</tr>
<tr>
<td>A4207</td>
<td>Syringe with needle, sterile 2 cc, each</td>
</tr>
<tr>
<td>A4208</td>
<td>Syringe with needle, sterile 3 cc, each</td>
</tr>
<tr>
<td>A4209</td>
<td>Syringe with needle, sterile 5 cc or greater, each</td>
</tr>
<tr>
<td>A4211</td>
<td>Supplies for self-administered injections</td>
</tr>
<tr>
<td>A4212</td>
<td>Non-coring needle or stylet with or without catheter</td>
</tr>
<tr>
<td>A4213</td>
<td>Syringe, sterile, 20 cc or greater, each</td>
</tr>
<tr>
<td>A4215</td>
<td>Needle, sterile, any size, each</td>
</tr>
<tr>
<td>A4221</td>
<td>Supplies for maintenance of drug infusion catheter, per week (list drug separately)</td>
</tr>
<tr>
<td>A4222</td>
<td>Infusion supplies for external drug infusion pump, per cassette or bag (list drugs separately)</td>
</tr>
<tr>
<td>A4230</td>
<td>Infusion set for external insulin pump, non-needle cannula type</td>
</tr>
<tr>
<td>A4231</td>
<td>Infusion set for external insulin pump, needle type</td>
</tr>
<tr>
<td>A4232</td>
<td>Syringe with needle for external insulin pump, sterile, 3cc</td>
</tr>
<tr>
<td>A4233</td>
<td>Replacement battery, alkaline (other than J cell), for use with medically necessary home blood glucose monitor owned by patient, each</td>
</tr>
<tr>
<td>A4234</td>
<td>Replacement battery, alkaline, J cell, for use with medically necessary home blood glucose monitor owned by patient, each</td>
</tr>
<tr>
<td>A4235</td>
<td>Replacement battery, lithium, for use with medically necessary home blood glucose monitor owned by patient, each</td>
</tr>
<tr>
<td>A4236</td>
<td>Replacement battery, silver oxide, for use with medically necessary home blood glucose monitor owned by patient, each</td>
</tr>
<tr>
<td>A4244</td>
<td>Alcohol or peroxide, per pint</td>
</tr>
<tr>
<td>A4245</td>
<td>Alcohol wipes, per box</td>
</tr>
<tr>
<td>A4246</td>
<td>Betadine or pHisoHex solution, per pint</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>A4247</td>
<td>Betadine or iodine swabs/wipes, per box</td>
</tr>
<tr>
<td>A4250</td>
<td>Urine test or reagent strips or tablets (100 tablets or strips)</td>
</tr>
<tr>
<td>A4252</td>
<td>Blood ketone test or reagent strip, each</td>
</tr>
<tr>
<td>A4253</td>
<td>Blood glucose test or reagent strips for home blood glucose monitor, per 50 strips</td>
</tr>
<tr>
<td>A4255</td>
<td>Platforms for home blood glucose monitor, 50 per box</td>
</tr>
<tr>
<td>A4256</td>
<td>Normal, low, and high calibrator solution/chips</td>
</tr>
<tr>
<td>A4258</td>
<td>Spring-powered device for lancet, each</td>
</tr>
<tr>
<td>A4259</td>
<td>Lancets, per box of 100</td>
</tr>
<tr>
<td>A9274</td>
<td>External ambulatory insulin delivery system, disposable, each, includes all supplies and accessories</td>
</tr>
<tr>
<td>A9275</td>
<td>Home glucose disposable monitor, includes test strips</td>
</tr>
<tr>
<td>E0607</td>
<td>Home blood glucose monitor</td>
</tr>
<tr>
<td>E0784</td>
<td>External ambulatory infusion pump, insulin</td>
</tr>
<tr>
<td>E2101</td>
<td>Blood glucose monitor with integrated lancing/blood sample</td>
</tr>
<tr>
<td>G0108</td>
<td>Diabetes outpatient self-management training services, individual, per 30 minutes</td>
</tr>
<tr>
<td>G0109</td>
<td>Diabetes outpatient self-management training services, group session (2 or more), per 30 minutes</td>
</tr>
<tr>
<td>J1815</td>
<td>Injection, insulin, per 5 units</td>
</tr>
<tr>
<td>J1817</td>
<td>Insulin for administration through DME (i.e., insulin pump) per 50 units</td>
</tr>
<tr>
<td>S5550</td>
<td>Insulin, rapid onset, 5 units</td>
</tr>
<tr>
<td>S5551</td>
<td>Insulin, most rapid onset (Lispro or Aspart); 5 units</td>
</tr>
<tr>
<td>S5552</td>
<td>Insulin, intermediate acting (NPH or LENTE); 5 units</td>
</tr>
<tr>
<td>S5553</td>
<td>Insulin, long acting; 5 units</td>
</tr>
<tr>
<td>S5560</td>
<td>Insulin delivery device, reusable pen; 1.5 ml size</td>
</tr>
<tr>
<td>S5561</td>
<td>Insulin delivery device, reusable pen; 3 ml size</td>
</tr>
<tr>
<td>HCPCS</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>S5565</td>
<td>Insulin cartridge for use in insulin delivery device other than pump; 150 units</td>
</tr>
<tr>
<td>S5566</td>
<td>Insulin cartridge for use in insulin delivery device other than pump; 300 units</td>
</tr>
<tr>
<td>S5570</td>
<td>Insulin delivery device, disposable pen (including insulin); 1.5 ml size</td>
</tr>
<tr>
<td>S5571</td>
<td>Insulin delivery device, disposable pen (including insulin); 3 ml size</td>
</tr>
<tr>
<td>S8490</td>
<td>Insulin syringes (100 syringes, any size)</td>
</tr>
<tr>
<td>S9140</td>
<td>Diabetic management program, follow-up visit to non-MD provider</td>
</tr>
<tr>
<td>S9141</td>
<td>Diabetic management program, follow-up visit to MD provider</td>
</tr>
<tr>
<td>S9145</td>
<td>Insulin pump initiation, instruction in initial use of pump (pump not included)</td>
</tr>
<tr>
<td>S9353</td>
<td>Home infusion therapy, continuous insulin infusion therapy; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem</td>
</tr>
<tr>
<td>S9455</td>
<td>Diabetic management program, group session</td>
</tr>
<tr>
<td>S9460</td>
<td>Diabetic management program, nurse visit</td>
</tr>
<tr>
<td>S9465</td>
<td>Diabetic management program, dietician visit</td>
</tr>
</tbody>
</table>

**HCPCS codes not covered for indications listed in the CPB:**

**Remote Glucose monitor** No specific code [e.g. Dexcom SHARE - no additional reimbursement provided], MiniMed Connect:

No specific code

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A4210</td>
<td>Needle-free injection device, each</td>
</tr>
<tr>
<td>A4257</td>
<td>Replacement lens shield cartridge for use with laser skin piercing device, each</td>
</tr>
<tr>
<td>A9280</td>
<td>Alert or alarm device, not otherwise classified [hypoglycemic wristband alarm (e.g., Sleep Sentry)]</td>
</tr>
<tr>
<td>C1788</td>
<td>Port, indwelling (implantable)</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>E0620</td>
<td>Skin piercing device for collection of capillary blood, laser, each</td>
</tr>
<tr>
<td>E2100</td>
<td>Blood glucose monitor with integrated voice synthesizer</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E08.00</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>E13.9</td>
<td></td>
</tr>
<tr>
<td>G25.82</td>
<td>Sti -man syndrome [indicated for GAD antibodies]</td>
</tr>
<tr>
<td>O24.011</td>
<td>Diabetes mellitus in pregnancy, childbirth, and the puerperium</td>
</tr>
<tr>
<td>O24.93</td>
<td></td>
</tr>
<tr>
<td>O99.810</td>
<td>Abnormal glucose complicating pregnancy, childbirth, and the puerperium</td>
</tr>
<tr>
<td>O99.815</td>
<td></td>
</tr>
</tbody>
</table>

**Continuous Glucose Monitoring Devices:**

**Short-term monitoring:**

**CPT codes covered if selection criteria are met:**

<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 [type 1 only see criteria]</td>
</tr>
<tr>
<td>95251</td>
<td>physician interpretation and report</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E08.00</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>E13.9</td>
<td></td>
</tr>
</tbody>
</table>

**Long-term monitoring:**

**HCPCS codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<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>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>S1030</td>
<td>Continuous noninvasive glucose monitoring device, purchase</td>
</tr>
<tr>
<td>S1031</td>
<td>Continuous noninvasive glucose monitoring device, rental, including sensor, sensor replacement, and download to monitor</td>
</tr>
<tr>
<td>S1034</td>
<td>Artificial pancreas device system (e.g., low glucose suspend [LGS] feature) including continuous glucose monitor, blood glucose device, insulin pump and computer algorithm that communicates with all of the devices</td>
</tr>
<tr>
<td>S1035</td>
<td>Sensor; invasive (e.g., subcutaneous), disposable, for use with artificial pancreas device system</td>
</tr>
<tr>
<td>S1036</td>
<td>Transmitter; external, for use with artificial pancreas device system</td>
</tr>
<tr>
<td>S1037</td>
<td>Receiver (monitor); external, for use with artificial pancreas device system</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met for age 25 and older:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E10.10</td>
<td>Type 1 diabetes mellitus</td>
</tr>
<tr>
<td>E10.9</td>
<td></td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met under age 25:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E10.641 - E10.649</td>
<td>Type 1 diabetes mellitus with hypoglycemia [with recurrent episodes of severe hypoglycemia (blood glucose less than 50 mg/dL) despite appropriate modifications in insulin regimen and compliance with frequent self-monitoring (at least four fingersticks per day)]</td>
</tr>
<tr>
<td>E10.65</td>
<td>Type 1 diabetes mellitus with hyperglycemia [with recurrent episodes of severe hypoglycemia (blood glucose less than 50 mg/dL) despite appropriate modifications in insulin regimen and compliance with frequent self-monitoring (at least four fingersticks per day)]</td>
</tr>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB:**
The above policy is based on the following references:


Disorder of pancreatic internal secretion, unspecified [nesidioblastosis]


50. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Use of intermittent or continuous interstitial fluid glucose monitoring in patients
with diabetes mellitus. TEC Assessment Program. Chicago, IL: BCBSA; December 2003; 17(2).


71. Australia and New Zealand Horizon Scanning Network
(ANZHSN). Continuous glucose monitoring devices. Horizon Scanning Report. Christchurch, NZ: New Zealand Health Technology Assessment (NZHTA); 2006. Available at:  


77. Patton Medical Devices, LP. I-Port Injection Port [website]. Austin, TX: Patton Medical Devices; 2007. Available at: http://www.i-port.com/  

78. U.S. Food and Drug Administration (FDA), Center for Biologics and Radiologic Health (CDRH). I-Port Injection Port. 510(k) Summary. 510(k) No. K052389. Rockville, MD: FDA; September 9, 2005. Available at:


91. The Juvenile Diabetes Research Foundation [JDRF] Continuous Glucose Monitoring Study Group;


110. Parrella A, Hiller J, Mundy L. Temptouch™ Infrared


Prioritising Summary. Adelaide, SA: Adelaide Health Technology Assessment (AHTA); 2009; 23.


144. Fierheller M, Sibbald RG. A clinical investigation into the relationship between increased periwound skin temperature and local wound infection in patients with chronic leg ulcers. Adv Skin Wound Care. 2010;23(8):369-379;


and safety]. Summary. CT09/2010. Barcelona, Spain: Catalan Agency for Health Information, Assessment and Quality (CAHIAQ); 2010.


151. Kushner RF, Cummings S. Medical management of patients after bariatric surgery. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed June 2012.

152. Adair JD, Ellsmere JC. Complications of bariatric surgery. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed June 2012.


157. NHIC, Corp. Local Coverage Determination (LCD) for Glucose Monitors (L11530). Durable Medical Equipment
Medicare Administrative Contractor (DME MAC)
Jurisdiction A. Hingham, MA: NHIC; revised November 1, 2012.


166. Sunehag A, Haymond MW. Pathogenesis, clinical features, and diagnosis of persistent hyperinsulinemic hypoglycemia of infancy. UpToDate [online serial].


173. Blue Cross Blue Shield Association (BCBSA), Technology Evaluation Center (TEC). Artificial pancreas device systems. TEC Assessment Program. Chicago, IL: BCBSA; May 2014;28(14).


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Amendment to
Aetna Clinical Policy Bulletin Number: CPB 0070
Diabetes Tests, Programs and Supplies

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania
Updated 05/2017