Health Technology Clinical Committee
Findings and Coverage Decision
Topic: **Glucose Monitoring for Insulin Dependent Individuals Under 19 Years of Age**
Meeting Date: **March 18th, 2011**
Final Adoption: **June 17th, 2011**

Number and Coverage Topic

20110318A – Glucose Monitoring for Insulin Dependent Individual Under 19 Years of Age

HTCC Coverage Determination

Self Monitoring Blood Glucose (SMBG) is **covered benefit**

Continuous Glucose Monitoring (CGM) is a **covered benefit with conditions**

HTCC Reimbursement Determination

❖ **Limitations of Coverage**

- Continuous Glucose Monitoring (CGM) is a covered benefit for diabetes mellitus (DM) patients under 19 using insulin when the following conditions are met:
  - Suffering from one or more severe episodes of hypoglycemia; or
  - Enrolled in an IRB approved trial

❖ **Non-Covered Indicators**

- N/A

❖ **Agency Contact Information**

Agency	Contact Phone Number
Labor and Industries	1-800-547-8367
Public Employees Health Plan	1-800-762-6004
Health and Recovery Services Administration	1-800-562-3022

Health Technology Background

The Glucose Monitoring topic was selected and published in December 2008 to undergo an evidence review process. The evidence based technology assessment report indicates that self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGM) are two techniques that persons with diabetes use at home to help them maintain blood glucose within a safe range. Intensive treatment with tight control of blood glucose has become the standard of care for diabetes. Such intensive treatment requires monitoring as part of that regimen: by knowing the blood sugar levels the patient or caregiver can adjust diet, exercise, and insulin appropriately.

Self-monitoring of blood glucose (SMBG), sometimes called intermittent monitoring, using meters which analyze small amounts of capillary blood on reagent-coated test stripes, provides immediate documentation of glycemic status. This allows one to implement strategies to address and avoid out of range glucose values. It provides only a snapshot of the blood glucose level and thus, cannot provide information on whether there is a trend toward higher or lower levels.

Minimally-invasive devices which measure interstitial fluid glucose concentration via sensors which have been inserted subcutaneously have become more widely available. These devices take samples every 1-20 minutes over the time that the device is worn. Such continuous glucose monitors (CGM) may download data to an insulin pump and/or are stored in a receiver device. CGMs may guide real-time adjustment of food and insulin. Frequent readings may assist patients in seeing if there is a trend toward increasing or decreasing glucose levels so that they can act accordingly. They may aid in identifying times of consistent hyperglycemia or increased risk of hypoglycemia. Some may sound an alarm based on specific targets values and rate of change of interstitial glucose which may facilitate initiation of the appropriate action(s) to avoid hyper- or hypoglycemic events.

The effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial. Several lines of evidence have suggested an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self-monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test. On the other hand, children and adolescents can be especially at risk for some diabetes related complications (e.g. hypoglycemia, ketoacidosis) recommended. Information about the best options for glucose monitoring in diabetic persons 18 and under, including evidence of efficacy and safety and cost; and correlation of frequency (including strip frequency and continuous monitoring) to improved outcomes is needed.

In November 2010, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed Glucose Monitoring report is 152 pages, and identified a relatively large amount of literature.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on March 18th, reviewed the report, including peer and public feedback, and heard public and agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at http://www.hta.hca.wa.gov under the committee section.

P.O. Box 42712 • Olympia, Washington 98504 • www.hta.hca.wa.gov • 360-923-2742 • FAX 360-923-2835 • TTY 360-923-2701

Committee Findings

Having considered the evidence based technology assessment report and the written and oral comments, the committee identified the following key factors and health outcomes, and evidence related to those health outcomes and key factors:

1. Evidence availability and technology features

The evidence based technology assessment report indicates:

- Diabetes mellitus or diabetes is a serious chronic disease characterized by elevation of blood glucose. The predominated form of diabetes in children is from an autoimmune disorder that destroys the pancreatic cells where insulin is made. There is no cure; insulin injections are required and the primary goals for treatment of youth with insulin requiring diabetes are to maintain plasma glucose and A1C levels as close to normal as possible. Diabetic ketoacidosis (very high glucose level) is the leading acute complication and can result in morbidity and mortality. A seminal diabetes study (DCCT) results suggest that maintaining near normal levels of A1C are ideal to minimize the risk of chronic complications, but the lower the A1C puts individuals at risk of severe hypoglycemia. Children and adolescents have challenges related to varying physical capability, physiological and psycho-social changes that influence metabolism and adherence to self care behaviors.
- Self monitoring of blood glucose has become a standard practice recommendation due to the link between good glycemic control and lower chronic complications; however, the method and optimal frequency of self-monitoring of blood glucose in patients remains controversial. Several lines of evidence have suggested an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self-monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test. On the other hand, children and adolescents can be especially at risk for some diabetes related complications. Information about the best options for glucose monitoring in diabetic persons 18 and under, including evidence of efficacy and safety and cost; and correlation of frequency (including strip frequency and continuous monitoring) to improved outcomes is needed.
- Self-monitoring of blood glucose (SMBG) uses meters to analyze small amounts of capillary blood on reagent-coated test strips to provide immediate documentation of glycemic status. This allows one to implement strategies to address and avoid out of range glucose values. It provides only a snapshot of the blood glucose level and thus, cannot provide information on whether there is a trend toward higher or lower levels. Continuous glucose monitors (CGM) are more recent technology where a minimally-invasive device is worn to measure interstitial fluid glucose concentration via sensors which have been inserted subcutaneously. These devices take samples every 1-20 minutes over the time that the device is worn. CGM is not approved for insulin dosing decisions, so individuals using CGM must still conduct SMBG several times a day.
- Evidence included in the technology assessment review was obtained through a structured, systematic search of the medical literature; economic studies; and clinical guidelines. 240 potentially relevant studies were identified; 49 were included; no economic studies found. The evidence is indirect because SMGB is note separately studied. Primary evidence for SMBG is 1 randomized control trial (DCCT) and 2 associated observational follow up (EDIC); 1 larger registry study and 7 cross-sectional studies. For CGM, 4 RCTs and JDRF's analysis were included, though data is not uniformly available for 18 and under.
- The evidence based technology assessment report identified six expert treatment guidelines and no National Coverage decision (NCD) policy addressing children.
- The committee also reviewed information provided by the state agencies, and public members; and heard comments from the evidence reviewer, clinical expert, HTA program, agency medical directors and the public.

2. Is the technology safe?

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is safe. Summary of committee considerations follows.

- The evidence based technology assessment report indicates that the strength of evidence of safety is moderate based on number and quality of studies. SGBM and CGM have no major adverse events or deaths. *(Adverse events from severe high and low glucose are described in efficacy).*
- The evidence based technology assessment report indicates that the primary issues for SGBM are from older studies that reported sore fingers and difficulty obtaining samples.
- The evidence based technology assessment report indicates that for CGM, primary issues from small RCT and observational studies included skin irritation (0%- 53%); sensor dislodging (10% - 13%); alarms interfering with daily routine (38%) and irritation with alarms (38% - 50%). The primary safety issue with CGMs are false alerts and missed alerts (false negatives); rates varied across blood glucose thresholds and devices – false negatives rates for hypoglycemia (below threshold) ranged from 14% to 75% and false negative rates for hyperglycemia (above threshold) ranged from 5% to 37%).

3. Is the technology effective?

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is effective. Summary of committee considerations follows.

- Efficacy of SMBG – the evidence based technology assessment report indicated that no studies evaluated current methods of SMBG testing alone or as an independent component of diabetes management. The Diabetes Complications and Control Trial (DCCT-1994) is the primary study of 195 patients aged 13 to 17 providing indirect evidence regarding the efficacy of SMBG as part of a package of comprehensive, intensive diabetes care, which included SMBG four or more times per day and education on how to use the information to adjust insulin, diet and exercise compared with the then standard of care (urine or SMBG once/day, only periodic insulin adjustment).
    - Mean A1c levels 8.06% for intensive care arm vs. 9.7% for conventional arm; a 61% risk reduction in sustained at least three step retinopathy in intensive arm; no difference in nephrology; no difference in ketoacidosis (18% vs. 20%); and a threefold higher risk of hypoglycemia resulting in coma/seizure in intensive care arm.
- Effectiveness of SMBG – the evidence based technology assessment report indicated indirect evidence on the effectiveness of SMBG is based on the Epidemiology of Diabetes Interventions and Complications (EDIC-2001) the observational follow-up to the DCCT at four and ten years with 175 patients. All participants in the conventional treatment arm were offered instruction in the use of intensive therapy and intensive treatment group patients were encouraged to continue such treatment. No significant differences between the groups identified except related to retinopathy at 4yr.
    - Mean A1c levels 8.38% for intensive arm vs. 8.45% in conventional at 4yr; and 8.2% for both groups at 10yr;
    - Retinopathy progression worse in 7% of intensive arm vs. 25% in conventional at 4yr and 51% for intensive arm vs. 53% in conventional at 10yr;
    - Severe hypoglycemia; macular edema; and nephropathy had no significant differences
- Efficacy and effectiveness by frequency or mode of test -- there were no clinical trials that directly evaluated the efficacy of SMBG frequency. Indirect evidence from the DCCT provides information with respect to frequency in that the intensive group was instructed to test at least four times per day compared with the conventional care groups once per day (see above).

The bulk of the evidence on efficacy of mode of self-monitoring comes from comparisons with continuous glucose monitors (CGM).

- CGM used with SMBG (for calibration and verification per FDA recommendations) was compared with SMBG alone; three RCTs form primary basis; overall *Strength of Evidence is low*. Data from one JDRF 2008 report on CGM (result stratified by age (n = 114, 8-14 year olds)) and one smaller Hirsch RCT (n = 40, 12-18 year olds) are primary studies. Another JDRF (2009) study has few outcomes stratified by age. In the JDRF studies, 84% of both CGM and SMBG groups used insulin pumps (which did not communicate with the CGM) and 100% of patients in the Hirsch study used pumps integrated with the CGM device in the CGM arm only. Different in population and study design preclude pooling of data.
  - Mean differences in HbA1C levels were not clinically or statistically significant in short term.
  - No study reported significant differences in episodes of hypoglycemia for CGM vs. SMBG.
  - 2 RCTs reporting on hyperglycemia reported no significant differences for CGM vs. SMBG.
  - Results on the effect of CGM vs. SMBG on medication or nutritional management conflicted: 2 studies reported significant differences in insulin doses where one study reported no change in insulin doses.
- There are currently no long-term comparative studies on these devices for evaluation of benefits, complications or diabetes-related co-morbidities on those ≤ 18 years old.

4. Special Populations?

- The evidence based technology assessment report reported one RCT and one large registry study directly assessed differential outcomes for either CGM or SMBG by age subpopulations. The overall strength of evidence is low.
- The evidence based technology assessment report included one RCT comparing CGM with SMBG in patients 8-14 years old and those 15-24 years old - each had similar results with regard to A1C and achieving targets for CGM and SMBG with no evidence of differential efficacy by age was demonstrated.
- The evidence based technology assessment report reported that there is limited evidence for differential effect of frequency of SMBG testing by age from one large registry study.
  - For 13-18 year olds an average improvement in A1C of 0.3% ± 0.011 for each additional SMBG was reported. This appears to apply up to tests five per day.
- In contrast, for ages 0-5 and 6-12, beyond one test per day, improvement in A1C was much less and averaged 0.04% ± 0.018 and 0.12% ± 0.010 respectively beyond one SMBG per day.

5. Is the technology cost-effective?

The committee discussed multiple key factors that were important for consideration in their overall decision on whether the technology has value and is cost-effective. Summary of committee considerations follows.

- The evidence based technology assessment report indicated that no evidence is available to assess the cost effectiveness of SMBG or CMG in persons with diabetes ≤18 years old who require insulin. No full economic studies which focused on the cost-effectiveness of CGM or the frequency of SMBG were found.

6. Medicare Decision and Expert Treatment Guidelines

Committee reviewed and discussed the expert guidelines as identified and reported in the technology assessment report.

- Centers for Medicare and Medicaid Services (CMS) – no NCD policy addressing children.
  - For adults, to be eligible for coverage of home blood glucose monitors and related accessories and supplies, the patient (or patient's care-giver) must meet all the following criteria:
    - Diagnosed with diabetes that is being treated by a physician
    - Glucose monitor and related supplies ordered by the treating physician with documentation of medical necessity for the prescribed frequency of testing
    - Successfully completed training or is scheduled to begin training in the use of these items
    - Capable of using the test results to assure appropriate glycemic control
    - Device is designed for home use
  - Supplies covered: Up to 100 test strips and lancets every month for beneficiaries who are insulin dependent and every 3 months for those who are non-insulin dependent, and one lancet device every 6 months for both indications.
- Guidelines – the evidence based technology assessment report identified six guidelines though a search of the *National Guideline Clearinghouse.*
  - American Diabetes Association (ADA), 2010 – *Frequency of self-monitored blood glucose (SMBG)*: SMBG in general has been extensively reviewed by the ADA and is recommended for patients of all ages with type 1 diabetes. The 2010 report did not specifically address frequency for children; however, in a statement published in 2005 by the ADA entitled Care of Children and Adolescents with Type 1 Diabetes it is recommended that SMBG be performed at least four times daily. *Continuous glucose monitoring (CGM):* CGM in conjunction with intensive insulin regimens can be a useful tool to lower A1c in selected adults (age ≥ 25 years) with type 1 diabetes. Although the evidence for A1c lowering is less strong in children, teens, and younger adults, CGM may be helpful in these groups. Success correlates with adherence to ongoing use of the device. CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes. *Glycemic goals:* consider age when setting glycemic goals in children and adolescents with type 1 diabetes, with less stringent goals for younger children.
  - Diabetes Coalition of California, California Diabetes Program, 2008 – this guideline addresses adults, children and adolescents with type 1 and type 2 diabetes mellitus. *SMBG testing:* typically test at least 4x / daily. *Lab exams:* A1c should be checked 1-2 times year if stable, quarterly if treatment changes or if not meeting goals. Target goal < 7.0% or < 1% above lab norms. For children, modify as necessary to prevent significant hypoglycemia. Furthermore, microalbuminuria should be checked beginning with puberty once the duration of diabetes is > 5 years unless proteinuria has been documented. *Self-care behaviors:* as appropriate for child's developmental stage.
  - International Society for Pediatric and Adolescent Diabetes (ISPAD), 2009 – In summary, SMBG is an essential tool in the optimal management of childhood and adolescent diabetes and, when financially possible, should be made available for all children with diabetes. The cost of BG monitoring is very expensive and in many countries the cost relative to the cost of living may make this technology unavailable. *Frequency of SMBG:* SMBG should be prescribed at a frequency to optimize each child's diabetes control, usually 4-6 times a day, because frequency of SMBG correlates with glycemic control. *CGM:* CGM devices are becoming available that may particularly benefit those with hypoglycemic unawareness, as the devices will alarm when glucose is below a specified range or with rapid rate of fall of glucose. *Glycemic goals:* the target

A1c for all child age-groups is recommended to be < 7.5%. Every child should have a minimum of one measurement of A1c per year. Ideally, there should be four to six measurements per year in younger children and three to four measurements per year in older children.

- National Institute for Health and Clinical Excellence (NICE), 2004 -- *SMBG:* who are trying to optimize their glycemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day. Should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care team. *CGM:* who have persistent problems with hypoglycemia awareness or repeated hypoglycemia or hyperglycemia should be offered CGM systems. *Glycemic goals:* should be encouraged to use blood glucose measurements for short-term monitoring of glycemic control. The target for long-term glycemic control is an A1c level of less than 7.5% without frequent disabling hypoglycemia and the child's care package should be designed to attempt to achieve this.
- American Association of Clinical Endocrinologists (AACE), 2010 – Personal CGM is recommended for patients with type 1 DM and following characteristics: hypoglycemic unawareness or frequent hypoglycemia; A1c over target, or with excess glycemic variability; requiring A1c lowering without increased hypoglycemia; during preconception or pregnancy. Personal CGM use is recommended for children and adolescents with type 1 DM who have achieved A1c levels less than 7.0%; youth with type 1 DM who have A1c levels of 7.0% or higher and are able to use the device on a near-daily basis. The following patients might be good candidates for personal CGM, and a trial of 2 to 4 weeks is recommended: youth who frequently monitor their blood glucose levels; committed families of young children (< 8 years old), especially if the patient is having problems with hypoglycemia.
- British Society of Pediatric Endocrinology, 2009 – *Proven clinical indication:* to lower A1c, when this remains above the individual's target despite optimized use of intensive insulin regimens. *Potential clinical indications – Diagnostic:* suspected nocturnal hypoglycemia and/or early morning hyperglycemia; suspected unrecognized hypoglycemia; A1c above individualized target despite intensified insulin therapy apparently optimized with self-monitoring; persistent disabling hypoglycemia despite conversion from MDI to CSII. *Potential clinical indications – Therapeutic:* further optimization of pump therapy regimens when A1c cannot be consistently lowered below 7.5%; protection against recurrent disabling hypoglycemia, and for those with hypoglycemia unawareness or debilitating fear of hypoglycemia.

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and agency and state utilization information. The committee concluded that the current evidence on Glucose Monitoring demonstrates that there is sufficient evidence to cover self-monitoring of blood glucose (SMBG) for insulin dependent individuals under the age of 19. The committee agreed that there is sufficient evidence on continuous glucose monitoring for insulin dependent individuals under the age of 19 to cover with conditions. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. Based on these findings, the committee voted to cover self-monitoring of blood glucose (SMBG). Based on these findings, the committee voted to cover with conditions continuous glucose monitoring (CGM).

Health Technology Clinical Committee Authority

Washington State's legislature believes it is important to use a scientific based, clinician centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority, through its Health Technology Assessment program to engage in a process for evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company and takes public input at all stages. Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State Health Technology Clinical Committee (HTCC) determines how selected health technologies are covered by several state agencies (RCW 70.14.080-140). These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases their decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Administrator.

P.O. Box 42712 • Olympia, Washington 98504 • www.hta.hca.wa.gov • 360-923-2742 • FAX 360-923-2835 • TTY 360-923-2701