JM Palmetto - GlycoMark Testing for Glycemic Control

CPT: 84378 (Sugars; Single Quantitative, each specimen), 84999 (Unlisted chemistry procedure)

CMS Policy for Alabama, Georgia, North Carolina, South Carolina, Tennessee, Virginia, and West Virginia

Local policies are determined by the performing test location. This is determined by the state in which your performing laboratory resides and where your testing is commonly performed.

Medically Supportive ICD Codes are listed on subsequent page(s) of this document.

Coverage Indications, Limitations, and/or Medical Necessity

This is a non-coverage policy for the GlycoMark® assay (aka 1,5-anhydroglucitol [1,5-AG]; developed by Nippon Kayaku, Co., Ltd).

Current Diabetes Testing

Hemoglobin A1C measurement, reflecting hemoglobin glycation over the erythrocyte life span, is proportional to the mean glucose concentration over the preceding 2-3 months. A1C testing is recommended by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) consensus guideline for pharmacotherapy to control hyperglycemia in type 2 diabetes.1 In addition to A1C, fasting plasma glucose is used by patients and physicians to monitor diabetes. However, recent evidence strongly suggests that control of post-prandial hyperglycemia (PPG) may be necessary to achieve A1C targets <7%.2

Several landmark clinical trials have convincingly demonstrated that individuals with diabetes are at increased risk of developing microvascular complications including retinopathy, nephropathy and neuropathy, as well as cardiovascular (CV) disease.3,4,5 The importance of tight glycemic control for protection against microvascular and CV disease in diabetes was established in the Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) study.6 The role of glycemic control on microvascular disease in type 2 diabetes was documented in the United Kingdom Prospective Diabetes Study (UKPDS).7 In addition, improving glycemic control improves microvascular outcomes, as illustrated by the findings of a meta-analysis of randomized trials (34,912 participants).8

Considerable data indicates that elevated PPG levels, even in the absence of fasting hyperglycemia, increases the risk for CV disease9,10,11 Numerous epidemiological studies have demonstrated a correlation between risk for CVD and both fasting and postprandial plasma glucose levels or A1C values.11The United Kingdom Prospective Diabetes Study (UKPDS)3,the Diabetes Control and Complications Trial (DCCT)5, the Action to Control Cardiovascular Risk in Diabetes (ACCORD)12, and the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE)13 were landmark controlled clinical trials that evaluated the benefits of intensive glucose control on diabetes complications. Both the DCCT and UKPDS primary intervention studies also demonstrated long-term macrovascular benefits (>10 year follow-up).6,14 These studies illustrate that intensive glycemic control early in the course of diabetes is important in achieving CV benefit and provides guidance in terms of stratification of patients' target glycemic control. The fact that postprandial glucose control is essential to optimize blood glucose levels has been confirmed by randomized controlled trials where therapeutic agents primarily target postprandial hyperglycemia.15,16,17

1,5-AG Assay

Measurement of serum 1,5-anhydroglucitol (1,5-AG) is thought to be a useful index of postprandial hyperglycemia, and is thought to be more robust than hemoglobin A1C (A1C) or fructosamine (used to evaluate glycemic control over 10-14 days).18,19 There is evidence that glycemic excursions, an aspect of diabetes control incompletely captured by A1C, may contribute to vascular damage independently of mean glucose concentration (A1C)20,21,22 Testing for 1,5-AG has been proposed to be an additional glycemic biomarker to assist clinicians in the management of glycemic control, particularly in patients with moderate to near-normal glycemic control to complement frequent self-monitoring or continuous monitoring of plasma glucose to confirm overall glycemic control.

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The 1,5-AG test measures the blood level of 1,5-anhydroglucitol, a compound that is ingested in food. Because the compound is not metabolized, a relatively constant blood level is maintained in individuals with blood glucose below 180 mg/dL via urinary excretion and reabsorption. In non-diabetic individuals, the rate of intake of 1,5-AG is matched by the daily excretion rate such that the serum levels and urinary excretion remain constant. When a diabetic's blood glucose exceeds 180 mg/dL, 1,5-AG reabsorption is competitively blocked by glucose and the serum level of 1,5-AG falls. Serum 1,5-AG decreases until glucose level drops below 180 mg/dL when 1,5-AG reabsorption resumes a steady rate. In brief, 1,5-AG levels are inversely proportional to the degree of hyperglycemia.

Proponents of serum 1,5-AG claim that testing reflects hyperglycemia over the past 2 weeks (inter-day excursions) and is recommended by the manufacturer for use in persons with diabetes and A1C <8% to help identify patients with frequent hyperglycemic excursions, and may be useful for estimating within-day glycemic excursion. They specify that serum 1,5-AG correlates with postprandial hyperglycemia in persons with diabetes and A1C <7% and is stated to be more strongly correlated with glucose variability as compared to A1C, fructosamine or glycated albumin over 2 to 3 days in persons with moderate glycemic control (A1C <8%). Data suggests that 1,5-AG is strongly inversely associated with A1C and fasting glucose in persons diagnosed with diabetes but is poorly correlated with fasting glucose and A1C in persons without diabetes. Multiple publications correlate various 1,5-AG end points with continuous glucose monitoring and show potentially improved correlation with glucose fluctuation and A1C in patients with diabetes and A1C <8% than other biomarkers.23,24,25,26,27,28 However, the number of studies and the quality of study correlations is poor. Appropriate clinical targets are unclear, as the strongest correlations are observed at the highest glucose concentrations which suggests that the utility of 1,5-AG may primarily be limited to persons with overtly elevated glucose.

In summary, the data to support the use of this test is based on showing correlations over short periods with other early glycemic markers (A1C, fructosamine, or glycated albumin) but is not specific to the intended use population. Comparative studies do not show that 1,5-AG is as good as a 2-hour post prandial blood glucose, or alternative biomarker. At the current time, the relationship of 1,5-AG to long term diabetic complications in a patient with A1C <8% is unknown. Furthermore, no prospective studies have shown that managing 1,5-AG in patients with an A1C of 6.5-8% reduces micro- or macrovascular complications. In addition, there are no definitive guidelines for using alternative biomarkers as adjuncts to standard markers of glycemia, such as A1C, fasting glucose, or self-monitoring blood glucose measures. Long-term prospective studies are lacking, and large cohort studies are warranted to determine whether alternative biomarkers have potential utility for early diagnosis, management of diabetes, and prevention of diabetic complications.

Due to the lack of clinical utility, 1,5-AG testing is not reasonable and necessary for the management of diabetes or the prevention of diabetic complications, and is not covered by Medicare.

Article Text:

The information in this article contains billing, coding or other guidelines that complement the Local Coverage Determination (LCD) for GlycoMark Testing for Glycemic Control L36761.

To receive a GlycoMark test denial, please submit the following claim information:

CPT® code 84378 or 84999

An Advance Beneficiary Notice (ABN) is not required for statutorily excluded services
For a voluntary issued ABN, append with GX modifier

To indicate a statutorily excluded service, append with a GY modifier

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There is a frequency associated with this test. Please refer to the Limitations or Utilization Guidelines section on previous page(s).

The ICD10 codes listed below are the top diagnosis codes currently utilized by ordering physicians for the limited coverage test highlighted above that are also listed as medically supportive under Medicare's limited coverage policy. **If you are ordering this test for diagnostic reasons that are not covered under Medicare policy, an Advance Beneficiary Notice form is required.**

Code	Description
N/A	N/A

Visit **QuestDiagnostics.com/MLCP** to view current limited coverage tests, reference guides, and policy information.

To view the complete policy and the full list of medically supportive codes, please refer to the CMS website reference www.cms.gov ►

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