Hemoglobin A1c

Policy Number: APEA – G2006 – Hemoglobin A1c
Initial Presentation Date: 7/01/2020
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Policy Description

Glycated hemoglobin (A1c) results from post-translational attachment of glucose to the hemoglobin in red blood cells at a rate dependent upon the prevailing blood glucose concentration. Therefore, their levels correlate well with glycemic control over the previous 8 to 12 weeks (McCulloch, 2018b). The measurement of hemoglobin A1c is recommended for diabetes management, including screening, diagnosis, and monitoring for diabetes and prediabetes.

Diabetes describes several heterogeneous diseases in which various genetic and environmental factors can result in the progressive loss of β-cell mass and/or function that manifests clinically as hyperglycemia (Skyler et al., 2017).

Related Policies

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Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual’s benefit coverage at the time of the request

1. Measurement of hemoglobin A1c MEETS COVERAGE CRITERIA for individuals with a diagnosis of either Type 1 or Type 2 diabetes as follows:
   a. Upon initial diagnosis to establish a baseline value and to determine treatment goals.
   b. Twice a year (every 6 months) in individuals who are meeting treatment goals and who, based on daily glucose monitoring, appear to have stable glycemic control.
   c. Quarterly in individuals who are not meeting treatment goals for glycemic control.
   d. Quarterly in individuals whose pharmacologic therapy has changed.
2. Measurement of hemoglobin A1c **MEETS COVERAGE CRITERIA** to help in detection and diagnosis of pre-diabetes or Type 2 diabetes in the following populations once every three years:

   a. asymptomatic individuals who are overweight or obese as defined by the ADA (BMI ≥25 kg/m² or BMI ≥23 kg/m² in Asian Americans) and who have one or more of the following risk factors:

      i. First degree relative with diabetes; OR

      ii. High-risk race/ethnicity (e.g., African American, Latino or Hispanics, Native American, Asian American, Pacific Islanders); OR

      iii. History of cardiovascular disease; OR

      iv. Hypertension (≥140/90 mmHg or on therapy for hypertension); OR

      v. HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L); OR

      vi. Women with polycystic ovary syndrome; OR

      vii. Physical inactivity; OR

      viii. Other clinical conditions associated with insulin resistance (e.g. Severe obesity, acanthosis nigricans)

   b. women who were previously diagnosed with gestational diabetes

3. For pre-diabetic individuals, screening for type 2 diabetes with either a fasting plasma glucose test or hemoglobin A1c test once a year **MEETS COVERAGE CRITERIA.**

4. Diabetes screening with a hemoglobin A1c determination **MEETS COVERAGE CRITERIA** once every 3 years for children (age 10 years and older OR after the onset of puberty, whichever occurs earlier) with the following characteristics:

   a. Overweight or obese as defined by ADA (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height); AND

   b. Must have one or more of the following additional risk factors:

      i. Maternal history of diabetes or gestational diabetes mellitus during the child’s gestation; OR

      ii. Family history of type 2 diabetes in first- or second-degree relative; OR

      iii. High-risk race/ethnicity (e.g., African American, Latino or Hispanics, Native American, Asian American, Pacific Islanders); OR

      iv. Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)

5. Measurement of hemoglobin A1c **MEETS COVERAGE CRITERIA** for pregnant individuals up to once per month during pregnancy.

6. Measurement of hemoglobin A1c **DOES NOT MEET COVERAGE CRITERIA** in the following circumstances:
a. in individuals who have been transfused within the past 120 days; OR
b. in individuals with a condition associated with increased red blood cell turnover, such as sickle cell disease, hemodialysis, recent blood loss or transfusion, or erythropoietin therapy; OR
c. in conjunction with measurement of fructosamine; OR
d. to diagnose the acute onset of type 1 diabetes in individuals with symptoms of hyperglycemia; OR
e. as a screening test for cystic fibrosis-related diabetes.

Scientific Background

Diabetes is a major health concern in the United States. According to the American Diabetes Association (ADA, 2017):

- Prevalence: In 2015, 30.3 million Americans, or 9.4% of the population, had diabetes. Approximately 1.25 million American children and adults have type 1 diabetes.
- Undiagnosed: Of the 30.3 million, 23.1 million were diagnosed, and 7.2 million were undiagnosed.
- Prevalence in seniors: The percentage of Americans age 65 and older remains high, at 25.2%, or 12 million seniors (diagnosed and undiagnosed).
- New Cases: 1.5 million Americans are diagnosed with diabetes every year.
- Prediabetes: In 2015, 84.1 million Americans age 18 and older had prediabetes.
- Deaths: Diabetes remains the 7th leading cause of death in the United States in 2015, with 79,535 death certificates listing it as the underlying cause of death, and a total of 252,806 death certificates listing diabetes as an underlying or contributing cause of death.

Diabetes can be classified into the following general categories:

- “Type 1 diabetes (due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency)”
- “Type 2 diabetes (due to a progressive loss of β-cell insulin secretion frequently on the background of insulin resistance)”
- “Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)”
- “Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)” (ADA, 2019a)
The diagnosis of diabetes mellitus is easily established when a patient presents with classic symptoms of hyperglycemia, which include polyuria, polydipsia, nocturia, blurred vision, and, infrequently, weight loss. The frequency of symptomatic diabetes has been decreasing in parallel with improved efforts to diagnose diabetes earlier through screening. Increasingly, the majority of patients are asymptomatic, and hyperglycemia is noted on routine laboratory evaluation, prompting further testing (McCulloch, 2018a).

Glycated hemoglobin A1c (also known as HbA1c, A1c, glycated hemoglobin, hemoglobin A1c) testing plays a key role in the management of diabetes. New hemoglobin enters circulation with minimal glucose attached. However, glucose irreversibly binds to hemoglobin based on the surrounding blood glucose concentration. Therefore, A1c is considered a measure of blood glucose level, albeit an indirect one. It is best correlated with the mean glucose level over the last 8 to 12 weeks as red blood cells experience significant turnover. Various factors may affect the reliability of A1c (atypical hemoglobins or hemoglobinopathies, chronic kidney disease, and such), but most assays have been standardized to the Diabetes Control and Complications Trial (DCCT) standard, which “estimated the mean blood glucose concentrations derived from seven measurements a day (before and 90 minutes after each of the three major meals, and before bedtime), performed once every three months and compared the average glucose concentration with A1c values in patients with type 1 diabetes” (McCulloch, 2018b).

The HbA1c assay provides information about the degree of long-term glucose control (Nathan, Singer, Hurxthal, & Goodson, 1984), and has been recommended for the diagnosis and monitoring of diabetes (ADA, 2010; IEC, 2009). Long term blood sugar control has been associated with decreased risk of retinopathy, nephropathy, neuropathy, and cardiovascular disease, peripheral arterial, cerebrovascular disease (Hanssen, Bangstad, Brinchmann-Hansen, & Dahl-Jorgensen, 1992) and myocardial fibrosis in adults with diabetes (Al-Badri et al., 2018). Higher HbA1c variability has been associated with higher all-cause mortality in patients with Type 2 Diabetes (Gu et al., 2018).

Analytical Validity

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working Group on HbA1c Standardization has developed a reference measurement system and the measurement of HbA1c is currently well-standardized (Hoelzel et al., 2004), and a sound reference system is in place to ensure continuity and stability of the analytical validity of HbA1c measurement (Weykamp et al., 2008). In contrast, plasma glucose concentration remains difficult to assay with consistent accuracy (Gambino, 2007). HbA1c has greater analytical stability (consistency with repetitive sample testing) and less day-to-day variability than either the fasting plasma glucose (FPG) or 2-h PG (Petersen, Jorgensen, Brandslund, De Fine Oliviarius, & Stahl, 2005; Rohlfing et al., 2002). For any given individual, the HbA1c exhibits little short-term biologic variability; its coefficient of variation (CV) is 3.6%, compared to FPG (CV of 5.7%) and 2-h PG (CV of 16.6%) (Malkani & Mordes, 2011; Selvin, Crainiceanu, Brancati, & Coresh, 2007).

A sample proficiency testing survey performed by the National Glycohemoglobin Standardization Program (NGSP) and College of American Pathologists (CAP) evaluated the accuracy of A1c assays. The survey found that “method-specific, between-laboratory CV’s [sic] ranged from 0.9% to 4.5%” and “approximately 91% of laboratories are using methods with CVs <3.5% at all four HbA1c levels.” The survey also noted the current pass limit was ±6%, but using a pass rate of 5%, 92.9% to 96.1% of labs passed (NGSP, 2019).

Clinical Validity

A1c, FPG, and 2-h PG measure different aspects of glycemia and are frequently discordant for diagnosing diabetes. A1c ≥6.5% identifies fewer individuals as having diabetes than glucose-based criteria; however, a recent study concluded that 12% of patients can be misclassified with respect to diabetes diagnosis due to laboratory instrument error in measuring glucose (Miller et
al., 2008). The New Hoorn Study analyzed the diagnostic properties of the A1c, using OGTT as the diagnostic criterion (van 't Riet et al., 2010). The analysis suggested that an A1c of 5.8% had a sensitivity of 72% and specificity of 91%. This compares with specificity of 24% and sensitivity of 99% for the A1c cut-point of 6.5%. On the other hand, the 6.5% cutpoint had a positive predictive value of 93%, compared with a positive predictive value of only 24% for a cut-point of 5.8% (Malkani & Mordes, 2011).

Cowie et al “examined prevalences of previously diagnosed diabetes and undiagnosed diabetes and high risk for diabetes using recently suggested A1c criteria in the U.S. during 2003–2006. We compared these prevalences to those in earlier surveys and those using glucose criteria.” 14611 individuals were included (completed a household interview) and classified for diagnosed diabetes and by A1c, fasting, and 2-h glucose challenge values. Diagnostic values for A1c were ≥6.5% for “undiagnosed” diabetes and 6%-6.5% for “high risk” of diabetes. The authors found that by these A1c diagnostic values, the “crude prevalence” of diabetes in adults older than 20 years was 20.4 million, of which 19% went undiagnosed based on A1c ≥ 6.5%. The authors then stated that the A1c criteria only diagnosed 30% of the undiagnosed diabetic group (Cowie et al., 2010).

Clinical Utility

Goodney et al evaluated the consistency of A1c testing of diabetes patients and its effect on cardiovascular outcomes. 1574415 Medicare patients with diabetes mellitus were included, and the consistency of testing was separated into three categories: “low (testing in 0 or 1 of 3 years), medium (testing in 2 of 3 years), and high (testing in all 3 years).” 70.2% of patients received high-consistency testing, 17.6% received medium-consistency, and 12.2% received low-consistency. Major adverse cardiovascular events (MACE) included “death, myocardial infarction, stroke, amputation, or the need for leg revascularization”. Low-consistency patients was associated with death or other adverse events (hazard ratio: 1.21). The authors concluded that “consistent annual hemoglobin A1c testing is associated with fewer adverse cardiovascular outcomes in this observational cohort of Medicare patients of diabetes mellitus (Goodney et al., 2016).”

The GOAL study (Al Mansari et al., 2018) used A1c to assess diabetes control in a real-world practice study aimed to assess predictive factors for achieving the glycemic hemoglobin A1c (HbA1c) at 6 months as targeted by the treating physician in adults with type 2 diabetes. 2704 patients with a mean A1c of 9.7% were enrolled. After 6 months, lower baseline A1c (≥ 8.5% vs <7%) was found to be a predictive factor for achieving glycemic control. The authors also observed “absolute changes in the mean HbA1c of −1.7% and −2% were observed from baseline to 6 and 12 months, respectively (Al Mansari et al., 2018).”

Mitsios et al evaluated the association between A1c and stroke risk. 29 studies (n=532779) were included. The authors compared the non-diabetic A1c range (<5.7%) to the diabetic range (≥6.5%) and found that the diabetic range was associated with a 2.15-fold increased risk of first-ever stroke. The pre-diabetes range of 5.7%-6.5% was also not associated with first-ever stroke. The authors also observed that for every 1% increase in A1c, the hazard ratio of first-ever stroke increased (1.12-fold for non-diabetic ranges, 1.17 for diabetic ones). This increased risk was also seen for ischemic stroke, with a hazard ratio of 1.49 for non-diabetic ranges and 1.24 for diabetic ranges (Mitsios, Ekinci, Mitsios, Churilov, & Thijs, 2018).

**Guidelines and Recommendations**

**The American Diabetes Association (ADA)**

The ADA publishes an extensive yearly guideline encompassing the standards of medical care in diabetes. The 2019 recommendations state:

*Screening for and diagnosis of diabetes (Chapter [Ch] 2) (ADA, 2019a):*
Criteria for testing for diabetes or prediabetes in asymptomatic adult:

- Testing should be considered in overweight or obese (BMI ≥25 kg/m² or ≥23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
  - First-degree relative with diabetes
  - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
  - History of CVD
  - Hypertension (≥140/90 mmHg or on therapy for hypertension)
  - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
  - Women with polycystic ovary syndrome
  - Physical inactivity
  - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

- Patients with prediabetes (A1c ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.

- Women who were diagnosed with GDM should have lifelong testing at least every 3 years.

- For all other patients, testing should begin at age 45 years.

- If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

- Diabetes may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-h plasma glucose (2-h PG) value after a 75-g oral glucose tolerance test (OGTT) or A1c criteria where A1c ≥6.5% (48 mmol/mol).

  - "To avoid misdiagnosis or missed diagnosis, the A1c test should be performed using a method that is certified by the NGSP and standardized to the Diabetes Control and Complications Trial (DCCT) assay. Grade B"

  - "Marked discordance between measured A1c and plasma glucose levels should raise the possibility of A1c assay interference due to hemoglobin variants (i.e., hemoglobinopathies) and consideration of using an assay without interference or plasma blood glucose criteria to diagnose diabetes. Grade B"

  - "In conditions associated with an altered relationship between A1c and glycemia, such as sickle cell disease, pregnancy (second and third trimesters and the postpartum period), glucose-6-phosphate dehydrogenase deficiency, HIV, hemodialysis, recent blood loss or transfusion, or erythropoietin therapy, only plasma blood glucose criteria should be used to diagnose diabetes. Grade B"

  - "Plasma blood glucose rather than A1c should be used to diagnose the acute onset of type 1 diabetes in individuals with symptoms of hyperglycemia. Grade E"

  - "To test for prediabetes and type 2 diabetes, fasting plasma glucose, 2-h plasma glucose during 75-g oral glucose tolerance test, and A1c are equally appropriate. Grade B"

  - "A1c is not recommended as a screening test for cystic fibrosis–related diabetes. Grade B"

- "Test for undiagnosed diabetes at the first prenatal visit in those with risk factors using standard diagnostic criteria."

- "Test for gestational diabetes mellitus at 24–28 weeks of gestation in pregnant women not previously known to have diabetes.” (ADA, 2019a)
For management of diabetes (Ch 2):

“The A1c test should be performed using a method that is certified by the NGSP (www.ngsp.org) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. Although point-of-care A1c assays may be NGSP certified, proficiency testing is not mandated for performing the test, so use of point-of-care assays for diagnostic purposes is not recommended but may be considered in the future if proficiency testing is performed, documented, and deemed acceptable (ADA, 2019a).”

Comorbidities (Ch 4)

“Individuals with HIV are at higher risk for developing prediabetes and diabetes on antiretroviral (ARV) therapies, so a screening protocol is recommended. The A1c test may underestimate glycemia in people with HIV and is not recommended for diagnosis and may present challenges for monitoring.” (ADA, 2019b)

Glycemic Targets (Ch 6)

- “Perform the A1c test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control).”
- “Perform the A1c test quarterly in patients whose therapy has changed or who are not meeting glycemic goals.”
- “Point-of-care testing for A1c provides the opportunity for more timely treatment changes.” (ADA, 2019c)

Children & Adolescents (Ch 13)

- The majority of patients diagnosed with autoimmune type 1 diabetes are under the age of 18. The recommendations concerning hemoglobin A1c for children and adolescents are as follows:
  - “An A1c target of <7.5% (58 mmol/mol) should be considered in children and adolescents with type 1 diabetes but should be individualized based on the needs and situation of the patient and family. Grade E”
  - “Fasting plasma glucose, 2-h plasma glucose during a 75-g oral glucose tolerance test, and A1c can be used to test for prediabetes or diabetes in children and adolescents. Grade B”
  - “Although A1c is not recommended for diagnosis of diabetes in children with cystic fibrosis or symptoms suggestive of acute onset of type 1 diabetes and only A1c assays without interference are appropriate for children with hemoglobinopathies, ADA continues to recommend A1c for diagnosis of type 2 diabetes in this population (ungraded)”
  - “If tests are normal, repeat testing at a minimum of 3-year intervals E, or more frequently if BMI is increasing. C” (ADA, 2019d)
- Concerning screening of asymptomatic children and adolescents (under the age of 18) for type 2 diabetes or prediabetes, the ADA recommends the following (ADA, 2019a):
  - Criteria: Overweight (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height) Grade A
  - Plus, one or more additional risk factors based on the strength of their association with diabetes as indicated by evidence grades:
    - Maternal history of diabetes or GDM during the child's gestation-Grade A
• Family history of type 2 diabetes in first- or second-degree relative-Grade A
• Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander)-Grade A
• Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)-Grade B

Pregnancy (Ch 14)

• “...although A1c may be useful, it should be used as a secondary measure of glycemic control in pregnancy, after self-monitoring of blood glucose.”

• “Due to increased red blood cell turnover, A1c is slightly lower in normal pregnancy than in normal nonpregnant women. Ideally, the A1c target in pregnancy is <6% (42 mmol/mol) if this can be achieved without significant hypoglycemia, but the target may be relaxed to <7% (53 mmol/mol) if necessary to prevent hypoglycemia”

• “Given the alteration in red blood cell kinetics during pregnancy and physiological changes in glycemic parameters, A1c levels may need to be monitored more frequently than usual (e.g., monthly).” (ADA, 2019e)

The American College of Physicians (ACP, 2018)
The ACP published guidelines (Qaseem et al., 2018) for glycemic control based on A1c which state:

Guidance Statement 1:
Clinicians should personalize goals for glycemic control in patients with type 2 diabetes on the basis of a discussion of benefits and harms of pharmacotherapy, patients' preferences, patients' general health and life expectancy, treatment burden, and costs of care.

Guidance Statement 2:
Clinicians should aim to achieve an HbA1c level between 7% and 8% in most patients with type 2 diabetes.

Guidance Statement 3:
Clinicians should consider deintensifying pharmacologic therapy in patients with type 2 diabetes who achieve HbA1c levels less than 6.5%.

The United States Preventive Services Task Force (USPSTF)
The USPSTF recommends screening overweight or obese adults ages 40-70 for abnormal blood glucose, with a grade B recommendation. In it, they recommend hemoglobin A1c as one of the screening tests (USPSTF, 2017)

World Health Organization (WHO)
The 2006 WHO criteria define diabetes as an FPG ≥126 mg/dL (7.0 mmol/L) or a two-hour, post-OGTT value ≥200 mg/dL (11.1 mmol/L). In 2011, the WHO concluded that an A1c value of ≥6.5 percent (48 mmol/mol) can be used as a diagnostic test for diabetes.

The Global Report on Diabetes (WHO, 2016) states that: "Glycated haemoglobin (HbA1c) is the method of choice for monitoring glycaemic control in diabetes. An advantage of using HbA1c is that the patient does not need to be in a fasting state. Ideally it should be measured twice a year in people with type 2 diabetes and more frequently in those with type 1 diabetes."
However, HbA1c testing is more costly than glucose measurement, and therefore less readily available. If HbA1c testing is not available, fasting or post-meal blood glucose is an acceptable substitute.”

The National Academy of Clinical Biochemistry (NACB)
The NACB guidelines (NACB, 2011) state:

• “Laboratories should use only Hb A1c assay methods that are certified by the National Glycohemoglobin Standardization Program (NGSP) as traceable to the DCCT reference. The manufacturers of Hb A1c assays should also show traceability to the IFCC reference method.”

• “Laboratories that measure HbA1c should participate in a proficiency-testing program, such as the College of American Pathologists (CAP) HbA1c survey, that uses fresh blood samples with targets set by the NGSP Laboratory Network.”

• “HbA1c testing should be performed at least biannually in all patients and quarterly for patients whose therapy has changed or who are not meeting treatment goals.”

• “HbA1c may be used for the diagnosis of diabetes, with values >6.5% being diagnostic. An NGSP-certified method should be performed in an accredited laboratory. Analogous to its use in the management of diabetes, factors that interfere with or adversely affect the Hb A1c assay will preclude its use in diagnosis.”

• “Point-of-care HbA1c assays are not sufficiently accurate to use for the diagnosis of diabetes.”

American Academy of Family Physicians (AAFP)
The AAFP published the revised Summary of Recommendations for Clinical Preventive Services in 2016 that stated that “the AAFP recommends screening for abnormal blood glucose as part of cardiovascular risk assessment in adults aged 40 to 70 years who are overweight or obese. The AAFP noted that “glucose abnormalities can be detected by measuring HgbA1c, fasting plasma glucose, or oral glucose tolerance test. Abnormal results should be confirmed.” The AAFP further stated that “there is limited evidence on the best rescreening interval for adults with normal results but screening every 3 years is a reasonable option.” (AAFP, 2016)

American Association of Clinical Endocrinologists/ American College of Endocrinology
The 2019 Consensus statement from the AACE/ACE on the Management of Type 2 Diabetes states:

• The hemoglobin A1c (A1c) target should be individualized based on numerous factors such as age, life expectancy, comorbid conditions, duration of diabetes, risk of hypoglycemia or adverse consequences from hypoglycemia, patient motivation, and adherence.

• An A1c level of ≤6.5% is considered optimal if it can be achieved in a safe and affordable manner, but higher targets may be appropriate for certain individuals and may change for a given individual over time.

• Therapy must be evaluated frequently (e.g., every 3 months) until stable using multiple criteria, including A1c, SMBG records (fasting and postprandial) or continuous glucose monitoring tracings, documented and suspected hypoglycemia events, lipid and BP values, adverse events (weight gain, fluid retention, hepatic or renal impairment, or CVD), comorbidities, other relevant laboratory data, concomitant drug administration, complications of diabetes, and psychosocial factors affecting patient care. Less frequent monitoring is acceptable once targets are achieved (Garber et al., 2019)
The 2015 guidelines (Garber et al., 2015) on Screening and Diagnosis for diabetes state:

- “Screening should be considered in the presence of risk factors for DM. (Grade C; BEL 3)”
- “Individuals at risk for DM whose glucose values are in the normal range should be screened every 3 years; clinicians may consider annual screening for patients with 2 or more risk factors. (Grade C; BEL 3)”
- “A1c level ≥6.5% may be used to diagnose DM. (Grade B; BEL 3)”
- “A1c should be measured at least twice yearly in all patients with DM and at least 4 times yearly in patients not at target.”
- “On the basis of these limitations, A1c measurement cannot be recommended as a primary method for diagnosing DM. The diagnosis of DM is best confirmed by 1 of the 3 established direct measures of plasma glucose, with A1c as a secondary criterion. In view of physiological changes in pregnancy that could affect glycated hemoglobin levels, A1C should not be used for GDM screening or diagnosis.”
- “A1C values between 5.5 and 6.4% inclusive should be a signal to do more specific glucose testing (Grade D; BEL 4). For prediabetes, A1c testing should be used only as a screening tool; FPG measurement or an oral glucose tolerance test (OGTT) should be used for definitive diagnosis (Grade B; BEL 2).” (Garber et al., 2015)

**State and Federal Regulations, as applicable**

The FDA has issued a 510(k) Premarket clearance to over 133 hemoglobin A1c test systems as a device used to measure the percentage concentration of hemoglobin A1c in blood (FDA, 2019). Measurement of hemoglobin A1c is used as an aid in the diagnosis of diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus.

Additionally, many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA’88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

**Applicable CPT/HCPCS Procedure Codes**

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<th>Code Description</th>
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<td>83036</td>
<td>Hemoglobin; glycosylated (A1c)</td>
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<td>83037</td>
<td>Hemoglobin; glycosylated (A1c) by device cleared by fda for home use</td>
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<td>82985</td>
<td>Glycated protein</td>
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*Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.*
Evidence-based Scientific References


**Policy Implementation/Update Information**

7/1/20  New Policy

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.