BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Quantose Impaired Glucose Tolerance (IGT) Test AHS - G2135

File Name:	quantose_impaired_glucose_tolerance_igt_test
Origination:	1/01/2019
Last CAP Review:	02/2020
Next CAP Review:	02/2021
Last Review:	07/2020

Description of Procedure or Service

Impaired glucose tolerance (IGT) refers to a condition in which the body cannot metabolize and regulate glucose properly (ADA, 2020).

Quantose Glucose Tolerance Test is a laboratory test developed by Metabolon (Metabolon, 2017a). According to Metabolon's website, "**QUANTOSE™ *IGT*** reflects the degree of impaired glucose tolerance in an individual. Impaired glucose tolerance (IGT) is a known risk factor for prediabetes. Our test is designed to easily differentiate IGT from normal glucose tolerance with only a single, fasted blood draw (Metabolon, 2017a)."

Diabetes is a major health concern in the United States. According to the Centers for Disease Control and Prevention (CDC, 2020):

- Prevalence: In 2018, 34.2 million Americans, or 10.5% of the population, had diabetes. Approximately 90%-95% of these cases are type 2.
- Undiagnosed: Of the 34.2 million, 26.9 million were diagnosed, and 7.3 million were undiagnosed.
- Prevalence in seniors: The percentage of Americans age 65 and older remains high, at 26.8%, or 12 million seniors (diagnosed and undiagnosed).
- New Cases: 1.5 million Americans are diagnosed with diabetes every year.
- Prediabetes: In 2018, 88 million Americans age 18 and older had prediabetes, a condition in which blood glucose levels are higher than normal but are not high enough for a diagnosis of diabetes. People with prediabetes are at increased risk for developing type 2 diabetes and for heart disease and stroke. Other names for prediabetes are impaired glucose tolerance and impaired fasting glucose.
- Deaths: Diabetes remains the 7th leading cause of death in the United States in 2017, with 83,564 death certificates listing it as the underlying cause of death, and a total of 270,702 death certificates listing diabetes as an underlying or contributing cause of death.
- Multiple comorbidities such as cardiovascular disease (including hyperlipidemia, coronary artery disease, and stroke), renal disease, (chronic renal insufficiency, dialysis and transplantation), infections, malignancy, and functional impairment are associated with uncontrolled diabetes.
- Total economic cost of diabetes care in the United States in 2017: $327 billion (CDC, 2020).

A diagnosis of diabetes is based on one of four abnormalities, one of which is an abnormal oral glucose tolerance test that measures IGT. This test assesses an individual's response to glucose and the rate which it clears from the blood, and it is used to diagnose diabetes, risk for prediabetes, or gestational diabetes (ADA, 2020). A set amount of glucose (usually 75 g) is ingested by the patient after a 9-hour fast, and a venipuncture is done 2 hours (±15 minutes) after ingestion (CDC, 2007). Then the glucose concentration is checked. A reading of 140 mg/dL to 199 mg/dL is considered "prediabetes", and >200 mg/dL is considered diagnostic for diabetes (ADA, 2020).

However, other tests exist for assessment of IGT. For example, Quantose IGT uses a proprietary algorithm to produce an "IGT score". This algorithm combines glucose and seven biomarkers, which are as follows: α-hydroxybutyric acid (AHB), 4-methyl-2-oxopentanoic acid (4MOP), oleic acid, linoleoylglycerophosphocholine (LGPC), β-hydroxybutyric acid (BHBA), serine, and pantothenic acid (vitamin B5) (Metabolon, 2017b).

Cobb et al used the data from the Relationship between Insulin Sensitivity and Cardiovascular Disease (RISC) Study to generate and validate the Quantose test. 1277 subjects from the RISC study were divided into a training set and a test set for algorithm development and validation. A total of 26 metabolites from this study were collated and investigated for potential inclusion into an insulin resistance algorithm along with body mass index (BMI) and insulin, and three metabolites (α-HB, L-GPC, and oleate) were incorporated into the algorithm. The test was validated with a 383-item sample, finding areas under the curve of 0.79 for insulin resistance and 0.70 for IGT progression. The investigators concluded that the Quantose test had clinical utility in the prediction of progression from normal glucose tolerance to impaired glucose tolerance and is superior to other simple baseline measures (fasting insulin, BMI, fasting glucose, HOMA-IR) in this regard. They further stated that the test may have value as an earlier predictor of prediabetes or Type 2 diabetes mellitus risk when compared with these traditional glycemic markers. The authors declared their potential conflicts of interest with respect to the research, authorship and/or publication of this article. The study was funded by Metabolon Inc. and 10 of the 13 authors of the study were full-time employees of Metabolon Inc (Cobb et al., 2013).

Tripathy et al evaluated the utility of Quantose IGT. The authors monitored changes in insulin sensitivity after pioglitazone therapy. 428 of the patients from the "ACT NOW" IGT study were placed on therapy and followed them for 2.4 years. The investigators found treatment lowered IGT progression to diabetes (hazard ratio: 0.25), and Quantose score was found to correlate with the Matsuda index of insulin sensitivity. Quantose score was also found to be progressively as higher across "closeout" glucose tolerance status (diabetes, IGT, normal glucose tolerance). The authors concluded that "Quantose MQ [score] may serve as a useful clinical test to identify and monitor therapy in insulin-resistant patients (Tripathy et al., 2015)."

Applicable Federal Regulations
This test is considered a laboratory developed test (LDT); developed, validated and performed by individual laboratories. 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.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Quantose impaired glucose tolerance (IGT) test is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Quantose Impaired Glucose Tolerance (IGT) Test is covered

Not applicable.

When Quantose Impaired Glucose Tolerance (IGT) Test is not covered

Quantose Impaired Glucose Tolerance (IGT) Test is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Policy Guidelines

Guidelines and Recommendations
There are no established guidelines or recommendations regarding the Quantose IGT test from any professional association and regulatory agencies. The USPSTF, AAFP, AACE, and ADA all recommend the OGTT as the primary evaluation of IGT (AAFP, 2017; ADA, 2020; Mechanick, Garber, Grunberger, Handelsman, & Garvey, 2018; Siu, 2015).

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 84999

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

AAFP. (2017). Summary of Recommendations for Clinical Preventive Services. Retrieved from https://www.aafp.org/patient-care/clinical-recommendations/all/diabetes-screening.html

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Metabolon. (2017a). QUANTOSE® IGT. Retrieved from https://www.metabolon.com/who-we-serve/clinical-consumer-applications/quantose-igt

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Siu, A. L. (2015). Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med, 163(11), 861-868. doi:10.7326/m15-2345

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Specialty Matched Consultant Advisory Panel review 2/2020

Policy Implementation/Update Information

1/1/2019	New policy developed. Quantose impaired glucose tolerance (IGT) test is considered investigational. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (lpr)
8/27/19	Removed coding table from Billing/Coding section per Avalon Q2 CAB 2019. No changes to policy statement. (lpr)
03/10/20	Specialty Matched Consultant Advisory Panel review 2/19/2020. No change to policy statement. (eel)
7/28/20	Reviewed per Avalon Q2 CAB. Medical Director review 7/2020. Updated Description, Policy Guidelines and References. No change to policy statement. (eel)