BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Use of Common Genetic Variants (Single-Nucleotide Variants) to Predict Risk of Nonfamilial Breast Cancer

Policy #: 422
Category: Laboratory

Latest Review Date: November 2019
Policy Grade: C

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*

    - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
    - *Furnished in a setting appropriate to the patient's medical needs and condition;*
    - *Ordered and furnished by qualified personnel;*
    - *One that meets, but does not exceed, the patient's medical need; and*
    - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service on or after June 22, 2010:

Blue Advantage will treat **testing for one or more single nucleotide variants (SNVs) to predict an individual's risk of breast cancer** as a **non-covered** benefit and as **investigational.**

Blue Advantage will treat the **BREVAGenplus® breast cancer risk tests as a non-covered benefit** and as **investigational** for all indications, including but not limited to use as a method of estimating individual patient risk for developing breast cancer.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Several single-nucleotide variants (SNVs), which are single base-pair variations in the DNA sequence of the genome, have been found to be associated with breast cancer and are common in the population but confer only small increases in risk. Commercially available assays test for a number of SNVs to predict an individual's risk of breast cancer relative to the general population. Some of these incorporate clinical information into risk prediction algorithms. Both types of test attempt to identify subjects at increased risk who may benefit from more intensive surveillance.

Clinical Genetic Tests

BREVAGenplus

BREVAGenplus evaluates breast cancer-associated single nucleotide variants (SNVs) identified in genome-wide association studies (GWAS). The first-generation test, BREVAGen, included seven SNVs. In a 2015 report, the test included over 70 susceptibility SNVs. Risk is calculated by combining individual SNV risks with the Gail model risk. BREVAGenplus has been evaluated for use in African-American, white, and Hispanic women age 35 years and older. BREVAGenplus does not detect known high-risk variants, e.g., in BRCA. According to the BREVAGenplus website, the test is

> "not applicable to women who are already at high risk of breast cancer including those that have a personal or extensive family history of breast and/or ovarian cancer, LCIS [lobular carcinoma in situ], DCIS [ductal carcinoma in situ], AH [atypical hyperplasia] or have thoracic RT [radiotherapy] under 30y. Any women with these risk factors are already at increased risk of breast cancer and should be screened and followed as such."

KEY POINTS:

The most recent literature update was performed through August 5, 2019.

Summary of Evidence

For individuals who are asymptomatic and at average risk of breast cancer by clinical criteria who receive testing for common SNVs variants that are associated with a small increase in risk for breast cancer, the evidence includes observational studies. Relevant outcomes are test validity, morbid events, and quality of life. Clinical genetic tests may improve the predictive accuracy of currently used clinical risk predictors. However, the magnitude of improvement is small, and clinical significance is uncertain. Whether potential harms of these tests due to false-negative and false-positive results are outweighed by the potential benefit associated with improved risk assessment is unknown. Evaluation of this technology is further complicated by the rapidly increasing numbers of SNVs that are associated with a small risk of breast cancer. Long-term prospective studies with large sample sizes are needed to determine the clinical validity and utility of SNV-based models for use in predicting breast cancer risk. The discrimination offered by the genetic factors currently known is insufficient to inform clinical practice. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

In its guidelines on genetic or familial high-risk assessment of breast and ovarian cancers (v.3.2019), the National Comprehensive Cancer Network (NCCN) notes the potential for multigene testing to identify intermediate penetrance (moderate risk) genes, but adds that "For many of these genes, there are limited data on the degree of cancer risk and there are no clear guidelines on risk management for carriers of pathogenic/likely pathogenic variants. Not all genes included on available multi-gene tests are necessarily clinically actionable." In the absence of evidence guiding follow-up to testing, including risk management strategies, NCCN recommends "that multi-gene testing is ideally offered in the context of professional genetic expertise, for pre- and post-test counseling."

American Society of Clinical Oncology

For breast cancer risk assessment, the American Society of Clinical Oncology recommends the Gail model or risk models for women with elevated risk based on family history (e.g., Claus et al [1994] or Tyrer et al [2004]).

U.S. Preventive Services Task Force Recommendations

No U.S. Preventive Services Task Force recommendations for SNV testing either in conjunction with or without consideration of clinical factors to predict breast cancer risk have been identified.

KEY WORDS:

Single nucleotide variants, (SNVs), deCODE, BreastCancer™ test, 23and me, deCODEme, Cancer Scan, Navigenics, BREVAGen, OncoVue, easyDNA, GenePlanet, Matrix Genomics, BREVAGenplus, common genetic variants, breast cancer risk, clinical genetic tests

APPROVED BY GOVERNING BODIES:

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). BREVAGenplus® (Phenogen Sciences, a subsidiary of Genetic Technologies, Melbourne, Australia) is available under the auspices of CLIA. Laboratories that offer laboratory-developed tests must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes: There is no specific CPT code for single nucleotide panel tests.

81479	Unlisted molecular pathology procedure
81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure

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POLICY HISTORY:

Adopted for Blue Advantage, May 2010
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Medical Policy Group, May 2011
Medical Policy Group, June 2012
Medical Policy Group, December 2012
Medical Policy Group, June 2013
Medical Policy Group, May 2015
Medical Policy Group, April 2016
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Medical Policy Group, November 2017
Medical Policy Group, October 2018 **(9)**: 2018 Updated to Description, Key Points, Approved by Governing Bodies & References. Added clarifying sentence to Coding Section "There is no specific CPT code for single nucleotide panel tests", no changes to codes. No changes to policy statement or intent. Added key words: common genetic variants, breast cancer risk, clinical genetic tests
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