Protocol

Use of Common Genetic Variants to Predict Risk of Nonfamilial Breast Cancer

(20463)

Medical Benefit		**Effective Date**: 01/01/11	**Next Review Date**: 09/14
Preauthorization	No	**Review Dates**: 09/10, 09/11, 09/12, 09/13	

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is not required but recommended if, despite this Protocol position, you feel the service is medically necessary; supporting documentation must be submitted to Utilization Management.*** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Description

Several s (SNPs), 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. Some commercially available assays test for several SNPs and combine results to predict an individual's risk of breast cancer relative to the general population. The intent of these assays is to identify those at increased risk who might benefit from more intensive surveillance.

Background

Rare, single gene variants conferring a high risk of breast cancer have been linked to hereditary breast cancer syndromes. Examples are mutations in BRCA1 and BRCA2. These, and a few others, account for less than 25% of inherited breast cancer. Moderate risk alleles, such as variants in the CHEK2 gene, are also relatively rare and apparently explain very little more of the genetic risk.

In contrast, several common SNPs associated with breast cancer have been identified primarily through genome-wide association studies of very large case-control populations. These alleles occur with high frequency in the general population, although the increased breast cancer risk associated with each is very small relative to the general population risk. Some have suggested that these common-risk SNPs could be combined to achieve an individualized risk prediction either alone or in combination with traditional predictors in order to personalize screening programs in which starting age and intensity would vary by risk. In particular, the American Cancer Society has recommended that women at high risk (greater than a 20% lifetime risk) should undergo breast magnetic resonance imaging (MRI) and a mammogram every year, while those at moderately increased risk (15% to 20% lifetime risk) should talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram.

At least 10 companies (Table) currently offer Internet-based testing for breast cancer risk profiles using SNPs. Most of these companies offer testing direct-to-consumers (DTCs), although Navigenics (Forest City, CA) and City of Hope (Duarte, CA) appear to offer testing only through physicians. The company does provide interested consumers with access to a network of physicians who are reported to be familiar with the company's test profile and who utilize the test.

The algorithms or risk models used for all the tests identified, except for those offered by deCODE (Reykjavik, Iceland), are proprietary and not described on company websites. In the five tests providing some information on the SNPs used for testing, these range from panels as small as six SNPs (Matrix Genomics, Santa Fe, NM) to as

large as 16 SNPs (deCODE). The Intergenetics Oncovue SNP-based test is profiled in a separate Protocol Non-BRCA Breast Cancer Risk Assessment [OncoVue]).

There appear to be two separate methods by which deCODE reports out risk for breast cancer. One is the deCODE BreastCancer™, test that includes a 16 SNP panel from which a risk assessment is derived for women of European ancestry. The second is the deCODEme Complete Scan for risk assessment of a broad assortment of diseases including breast cancer. A table in promotional material for this test suggests the risk levels differ based on ancestry with 17 SNPs of interest for patients of European descent, six for patients of Asian descent, and one for patients of African descent. It is not clear how or if deCODE uses this information in its Complete Scan report.

A list of companies offering DTC genetic testing for various diseases including breast cancer is maintained by the Genetics and Public Policy Center, available online at: http://www.dnapolicy.org/news.release.php?action=detail&pressrelease_id=137. However, this has not been updated since May 2010, and at least three of the companies on this list are no longer providing breast cancer testing.

Table. Tests for Breast Cancer Susceptibility Using SNP-Based Risk Panels.

Company	Location	Test Offered Direct-to-Consumer	Number of SNPs Used in Risk Panel
23andme	Mt. View, CA	Yes	7
City of Hope	Duarte, CA	No	7
deCODE	Reykjavik, Iceland	Yes	deCode BreastCancer – 16; deCODE Complete Scan – 16
easyDNA	Elk Grove, CA	Yes	ND
GenePlanet	Dublin, Ireland	Yes	15
Matrix Genomics	Santa Fe, NM	Yes	6
MediChecks	Nottingham, UK	Yes	ND
Navigenics	Forest City, CA	No*	ND
Pathway Genomics	San Diego, CA	Yes	ND
The Genetic Testing Laboratories	Las Cruces, NM	Yes	ND

ND – not described

*Consumers are referred to a network of providers for testing

Regulatory Status

No test combining the results of SNPs to predict breast cancer risk has been approved or cleared by the U.S. Food and Drug Administration (FDA). These are offered as laboratory-developed tests; that is, tests developed and used at a single testing site. Laboratory developed tests, as a matter of enforcement discretion, have not been traditionally regulated by FDA in the past. They do require oversight under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), and the development and use of laboratory developed tests is restricted to laboratories certified as high complexity under CLIA.

The FDA appears to be in the process of considering a change in its regulatory posture toward this group of DTC genetic tests (available online at: http://www.genomicslawreport.com/index.php/2010/07/21/14-more-fda-letters/). The FDA has met with many of the companies listed in the Table and has sent out letters indicating the belief that premarket submissions are warranted.

On July 19-20, 2010, the FDA held an open public meeting to allow stakeholders to comment on this issue. The FDA has not announced its final decisions about regulatory policy in the area, and so future regulatory requirements remain unclear.

Under the current regulatory program, CLIA requires that laboratories demonstrate the analytical validity of the tests they offer. However, there is no requirement for a test to demonstrate either clinical validity or clinical utility. Some states (e.g., New York) have chosen to regulate DTC laboratories. Because these reviews are not public, it is not possible to determine what scientific standard is being applied to them.

Related Protocols:

Genetic Testing for Hereditary Breast and/or Ovarian Cancer

Non-BRCA Breast Cancer Risk Assessment (e.g., OncoVue)

Corporate Medical Guideline

Testing for one or more single nucleotide polymorphisms (SNPs) to predict an individual's risk of breast cancer is considered **investigational**.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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