Harmony Behavioral Health, Inc.

Harmony Behavioral Health of Florida, Inc.

Harmony Health Plan of Illinois, Inc.

HealthEase of Florida, Inc.

'Ohana Health Plan, a plan offered by
WellCare Health Insurance of Arizona, Inc.

WellCare Health Insurance of Illinois, Inc.

WellCare Health Insurance of New York, Inc.

WellCare Health Plans of New Jersey, Inc.

WellCare of Florida, Inc.

WellCare of Connecticut, Inc.

WellCare of Georgia, Inc.

WellCare of Kentucky, Inc.

WellCare of Louisiana, Inc.

WellCare of New York, Inc.

WellCare of Ohio, Inc.

WellCare of Texas, Inc.

WellCare Prescription Insurance, Inc.

Genetic Testing for Susceptibility to Breast and Ovarian Cancer (BRCA1 and BRCA 2)

Policy Number: HS-113

Original Effective Date: 7/2/2009

Revised Date(s): 7/28/2010; 8/2/2011

DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

BACKGROUND

Two major breast cancer predisposition genes, known as the breast cancer 1 susceptibility gene (*BRCA1*) and breast cancer 2 susceptibility gene (*BRCA2*), have been implicated in up to 40% of hereditary breast cancers, and it is estimated that mutations in *BRCA1* and *BRCA2* account for 5% to 10% of all breast cancers. Both *BRCA* genes are very large, and researchers have identified more than 140 mutations. However, whether each of these mutations confers an equivalent risk of breast cancer, if any, is not known. The most commonly detected mutations are a deletion of adenine and guanine (185delAG) and an insertion of cytosine (5382insC) in the *BRCA1* gene and a deletion of thymine (6174delT) in the *BRCA2* gene. The combined frequency of these three mutations exceeds 2% in the Ashkenazi Jewish population. These mutations have been referred to as “founder” mutations since they can theoretically be traced back to a single founder.

Genetic testing for inherited susceptibility to breast cancer involves three distinct phases: (1) the pre-analytic phase, during which an individual trained in medical genetics determines which genetic test, if any, is appropriate and provides information to the patient; (2) the analytic phase, which involves molecular analysis of the patient’s deoxyribonucleic acid (DNA); and (3) the post-analytic phase, which involves the reporting and interpretation of results. During the pre-analytic phase, a qualified genetic counselor provides information regarding the disease, assesses the individual’s risk, and describes potential implications of positive and negative test results. The counselor establishes an individual’s pedigree through careful documentation of the family history of cancer, other diseases, developmental and congenital abnormalities, and a history of miscarriages. In addition, a personal medical history is taken and a physical examination performed on the individual. The risk of cancer susceptibility and options for surveillance, prevention, and treatment, as well as the predictive value of the DNA test results is discussed. Additionally, there should be a discussion of the pros and cons of testing, including the potential for discrimination in insurance coverage and employment, as well as the possible psychological ramifications of either a positive or negative test result on the individual and family members. After a period of reflection, written consent is obtained prior to collection of the blood sample for DNA testing.

There are a number of molecular techniques used to detect *BRCA1* and *BRCA2* gene mutations; full nucleotide screening, allele-specific oligonucleotide (ASO) hybridization, and protein truncation assays are most commonly used. Full nucleotide screening involves sequencing of the entire protein-coding regions of both *BRCA1* and *BRCA2*. Although full nucleotide screening is currently considered the gold standard of genetic testing for the susceptibility of breast cancer because it can detect a single point mutation, it may not detect large deletions or mutations that lie far away from the protein-coding regions.
ASO is designed for patients with a known *BRCA* mutation in the family. The test directly sequences a small portion of the gene to determine if the patient is a carrier of a specific mutation. If the single-site analysis is negative, the patient has not inherited the specific mutation associated with their family. It is rare that more than one mutation exists in a family; however, in this case, a negative single-site analysis test would only rule out the specific gene mutation for which the patient was tested. ASO may also be used to detect three mutations that are common in the Ashkenazi Jewish population. Although these mutations occur frequently within this population, Ashkenazi individuals may carry other mutations that would not be detected through this type of analysis. Protein truncation assays detect shortened protein products. This indicates the presence of a mutation that may confer an increased risk for breast cancer. Protein truncation assays are very accurate for detecting shortened proteins but will not detect proteins of normal length that may have aberrant sequences.

Women who have a positive test for a *BRCA* gene mutation can choose from a number of options; primary prevention strategies include prophylactic mastectomy and/or prophylactic oophorectomy, or chemoprevention with a drug such as tamoxifen that inhibits the development of breast cancer. Secondary prevention measures provide surveillance for early cancers, and include annual screening mammography, clinical breast examination, and breast self-examination, although breast self-examination has not been shown to reduce the numbers of deaths due to breast cancer and is not generally recommended as a replacement for clinical examination by a health professional (Hayes, 2002).

POSITION STATEMENT

Genetic testing for susceptibility to breast or ovarian cancer (BRCA1 and BRCA2) **in adults is considered medically necessary** when ANY of the following criteria is met:

- Biologically-related member from a family with a known BRCA1 or BRCA2 mutation; **OR,**
- Personal history of breast cancer and **ANY** of the following;

  a. Diagnosed at age 40 or younger; **OR,**
  b. Diagnosed at age 50 or younger and **EITHER** of the following is present:
     1. there is at least one close blood relative with breast cancer at age 50 or younger; **OR;**
     2. there is at least one close blood relative with epithelial ovarian cancer

  OR,

  c. Diagnosed with two breast primaries (includes bilateral disease or cases where there are two or more clearly separate ipsilateral primary tumors) and **EITHER** of the following is present:
     1. there is at least one close blood relative with breast cancer at age 50 or younger; **OR,**
     2. there is at least one close blood relative with epithelial ovarian cancer

  d. Diagnosed at any age and there are at least two close blood relatives with breast cancer or epithelial ovarian cancer at any age; **OR,**
  e. Close male blood relative with breast cancer; **OR,**
  f. Personal history of epithelial ovarian cancer; **OR,**
  g. A member of ethnicity associated with higher mutation frequency (e.g. founder populations of Ashkenazi Jewish, Icelandic, Swedish Hungarian or other)

- Personal history of epithelial ovarian cancer; **OR,**
- Personal history of male breast cancer particularly if **ONE** or more of the following is also present:

  a. One or more close male blood relative with breast cancer; **OR,**
  b. One or more close female blood relative with breast or epithelial ovarian cancer

OR,

- Family history only with a close family member meeting any of the above criteria

Genetic testing for susceptibility to breast or ovarian cancer (BRCA1 and BRCA2) in adults **is considered NOT medically necessary** in the following circumstances:

- Genetic screening in the general population; **OR,**
- Testing of members with no personal history of breast or ovarian cancer, except as noted above; **OR,**
- Testing of members under 18 years of age

NOTE: A close blood relative/close family member is defined as a first-, second-, or third-degree relative; this includes any of the following biologically-related individuals: a parent, full sibling, half sibling, child, grandparent, great-grandparent, grandchild, aunt, great aunt, uncle, great uncle, nephew, niece, or first cousin.

CODING

CPT®* Codes

83080 b-Hexosaminidase, each assay
83890 Molecular diagnostics; molecular isolation or extraction, each nucleic acid type (i.e., DNA or RNA)
83891 Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type, i.e. DNA or RNA)
83892 Molecular diagnostics; Enzymatic digestion, each enzyme treatment
83893 Molecular diagnostics; dot/slot blot production, each nucleic acid preparation
83894 Molecular diagnostics; separation by gel electrophoresis (e.g. agarose, polyacrylamide), each nucleic acid preparation
83896 Molecular diagnostics; nucleic acid probe, each
83897 Molecular diagnostics; nucleic acid transfer (eg Southern, Northern), each nucleic acid preparation
83898 Molecular diagnostics; amplification of patient nucleic acid, each nucleic acid sequence
83900 Molecular diagnostics; amplification, target, multiplex, first 2 nucleic acid sequences
83901+ Molecular diagnostics; amplification, target, multiplex, each additional nucleic acid sequence beyond 2
+ List separately in addition to code for primary procedure.
83902 Molecular diagnostics; reverse transcription
83903 Molecular diagnostics; mutation scanning, by physical properties, (eg, single strand conformational polymorphisms {SSCP}, heteroduplex, denaturing gradient gel electrophoresis {DGGE}, RNA'ase A), single segment, each
83904 Molecular diagnostics; mutation identification by sequencing, single segment, each segment
83905 Molecular diagnostics; mutation identification by allele specific transcription, single segment, each segment
83906 Molecular diagnostics; mutation identification by allele specific translation, single segment, each segment
83907 Molecular diagnostics; lysis of cells prior to nucleic acid extraction, (e.g., stool specimens, paraffin embedded tissue) each specimen
83908 Molecular diagnostics; signal amplification of patient nucleic acid, each nucleic acid sequence
83909 Molecular diagnostics; separation and identification by high resolution technique (eg, capillary electrophoresis) each nucleic acid sequence
83912 Molecular diagnostics; interpretation and report
83913 Molecular diagnostics; RNA stabilization
83914 Mutation identification by enzymatic ligation or primer extension, single segment, each segment (e.g., oligonucleotide ligation assay {OLA}, single base chain extension {SBCE}, or allele-specific primer extension {ASPE})
96040 Medical genetics and genetic counseling services, each 30 minutes face to face with patient/family

ICD-9-CM Procedure Codes - No applicable codes

HCPCS Codes*

S0265 Genetic counseling, under physician supervision, each 15 minutes
S3818 Complete gene sequence analysis; BRCA1 gene
S3819 Complete gene sequence analysis; BRCA2 gene
S3820 Complete BRCA1 and BRCA2 gene sequence analysis for susceptibility to breast and ovarian cancer
S3822 Single mutation analysis (in individuals with a known BRCA1 and BRCA2 mutation in the family) for susceptibility to breast and ovarian cancer
S3823 Three-mutation BRCA1 and BRCA2 analysis for susceptibility to breast and ovarian cancer in Ashkenazi individuals

***S- Codes are NON COVERED FOR MEDICARE – Refer to HCPCS Level II Temporary National Codes**

Covered ICD-9-CM Diagnosis Codes

174.0 - 174.9	Malignant Neoplasm of Female Breast
175.0 - 175.9	Malignant Neoplasm of Male Breast
183.0	Malignant Neoplasm of Ovary
233.0	Carcinoma in Situ of Breast
236.2	Neoplasm of Uncertain Behavior of the Ovary
238.3	Neoplasm of Uncertain Behavior of Breast
V10.3	Personal History of Malignant Neoplasm, Breast - Female or Male
V16.3	Family History of Malignant Neoplasm, Breast - Female or Male
V16.41	Family History of Malignant Neoplasm, Ovary

Non-Covered ICD-9-CM Diagnosis Codes

V84.01	Genetic Susceptibility to Malignant Neoplasm of Breast
V84.02	Genetic Susceptibility to Malignant Neoplasm of Ovary

***Current Procedural Terminology (CPT) 2010 American Medical Association: Chicago, IL.®©**

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Government Agencies, Professional and Medical Organizations

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HISTORY AND REVISIONS

Date	Action
12/1/2011	• New template design approved by MPC.
8/2/2011	• Approved by MPC. No changes.