



**HER-2/neu STATUS TESTING
IN BREAST CANCER
HS-121**



Harmony Behavioral Health, Inc.

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**HER-2/neu Status Testing
in Breast Cancer**

Policy Number: HS-121

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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

The amplification and over-expression of the HER-2/*neu* gene, also known as the *c-erbB-2* gene, has been detected in 20% to 30% of breast cancers. Alterations of this gene or an increase in gene products in breast cancer specimens are associated with shorter survival rates and a higher likelihood of disease recurrence and death. The accurate identification of patients with the gene alteration would allow them to be targeted for more aggressive therapy. Such alterations have also been associated with higher or lower response rates to specific anticancer therapies, potentially allowing physicians to select treatments for individual patients, which have the greatest likelihood of success for that individual. In particular, one therapy (trastuzumab) specifically targets HER-2/*neu* gene products and is only appropriate for members with alterations in this gene.

Various methods have been used to detect the HER-2/*neu* gene and its products in archival tissue specimens, including: gene expression analysis by Western blot testing or immunohistochemistry; measurement of messenger RNA (mRNA) levels by Northern blot analysis; and the direct measurement of gene amplification by Southern blot testing. At present, the two most commonly used methods for evaluating HER-2/*neu* status in a clinical setting are immunohistochemistry (IHC), which measures the over-expression of HER-2/*neu* gene products, and fluorescence in situ hybridization (FISH), which detects amplification of the gene itself. Chromogenic in situ hybridization (CISH) is a much newer technology and is still being tested, but is believed to have great potential, since it combines the advantages of the other two methods (from Hayes, 2004).

Algorithm for HER2 Testing

Positive for HER2 is either IHC HER2 3+ (defined as uniform intense membrane staining of > 30% of invasive tumor cells) or FISH amplified (ratio of *HER2* to CEP17 of > 2.2 or average *HER2* gene copy number > six signals/nucleus for those test systems without an internal control probe)

Equivocal for HER2 is defined as either IHC 2+ or FISH ratio of 1.8-2.2 or average *HER2* gene copy number four to six signals/nucleus for test systems without an internal control probe

Negative for HER2 is defined as either IHC 0-1+ or FISH ratio of <1.8 or average *HER2* gene copy number of < four signals/nucleus for test systems without an internal control probe.

POSITION STATEMENT

The testing of breast cancers for HER-2/*neu* gene amplification or for over-expression of the protein produced by HER-2/*neu* **is considered medically necessary** in conjunction with standard histopathological and clinical indicators of disease prognosis in order to:

- Stratify members into low- and high-risk categories for recurrence and disease-related death; **OR**,
- Identify members who might benefit from treatment with trastuzumab (Herceptin®); **OR**,
- To predict response to different chemotherapy regimens.

The following tests **are considered medically necessary** for the determination of HER-2/*neu* status in primary invasive breast cancer with negative axillary lymph nodes, positive axillary lymph nodes, or distant metastases, when test results will be used for determining prognosis and/or treatment planning:

1. Immunohistochemistry (IHC) testing **IF**:

- Performed by trained personnel; **AND**,
- The test has been calibrated against fluorescence in situ hybridization (FISH) or some other known

standard; **AND**,

- If equivocal cases are referred for FISH testing (see background section for more detail on equivocal results)

2. Fluorescence in situ hybridization (FISH) **IF**:

- Performed by trained personnel according to manufacturers standards; **AND**,
- Used only after an IHC test has been performed and the IHC results are equivocal

NOTE: Equivocal FISH samples should be confirmed through additional cell counts or by repeating the FISH test. If additional FISH analysis proves equivocal, confirmatory IHC testing is recommended.

The following tests **are considered experimental and investigational** in nature:

1. Chromogenic in situ hybridization (CISH)
2. HERmark™ Breast Cancer Assay (Monogram Biosciences)

CODING

Covered CPT® Codes

- 88360** Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, each antibody; manual
- 88361** Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, each antibody; using computer-assisted technology

Non-Covered CPT® Codes – (The following tests are considered experimental and investigational in nature).

- 84999** CISH -Chromogenic in situ hybridization
- 84999** HERmark™ Breast Cancer Assay (Monogram Biosciences)

ICD-9-CM Procedure Codes - No applicable codes

HCPCS Codes - No applicable codes

Covered ICD-9-CM Diagnosis Codes

- 174.0 - 175.9** Malignant neoplasm of breast
- 217** Benign neoplasm of breast
- 231.2** Carcinoma in situ of bronchus and lung
- 233.0** Carcinoma in situ of breast
- 238.3** Neoplasm of uncertain behavior of breast
- 239.3** Neoplasm of unspecified nature of breast
- V76.10** Breast screening for malignant neoplasms, unspecified
- V76.19** Other screening breast examination for malignant neoplasms
- 795.81** Elevated carcinoembryonic antigen [CEA] Cancer antigen 125 (CA 125)

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

REFERENCES

Peer Reviewed

1. Hayes Directory. Her-2/neu Status Testing Systems. May 30, 2004.

Government Agencies, Professional and Medical Organizations

1. Centers for Medicare and Medicaid Services (CMS), Local Coverage Determination (LCD) Trastuzumab (Herceptin) (L28998). First Coast Service Options, Inc. Feb. 16, 2009.
2. IHC Tests (ImmunoHistoChemistry). www.breastcancer.org. Dec. 8, 2008.
3. Journal of Oncology Practice. Guideline Summary: American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Human Epidermal Growth Factor Receptor HER2 Testing in Breast Cancer. Volume 3 Issue 1. 2007.

HISTORY AND REVISIONS

Date	Action
12/1/2011	<ul style="list-style-type: none">• New template design approved by MPC.
8/2/2011	<ul style="list-style-type: none">• Approved by MPC. No changes.