



**GENETIC ASSAY FOR BREAST CANCER  
(ONCOTYPE DX™)  
HS-079**



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**Genetic Assay for Breast  
Cancer (Oncotype™)**

**Policy Number: HS-079**

**Original Effective Date: 2/2/2009**

**Revised Date(s): 2/26/2010; 2/26/2011**

**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**

According to the American Cancer Society, nearly 213,000 new cases of breast cancer will be diagnosed in the United States in 2006 and almost 41,000 women will die of the disease. One factor that affects prognosis is whether or not the breast cancer has spread to the axillary lymph nodes. Over half of breast cancer patients have lymph node-negative (LN-) disease and are likely to remain free of tumor; however, disease recurs in about 30% of women with node-negative disease. Other prognostic factors such as tumor size, tumor grade, hormone receptor status, age, histology, and cell growth characteristics can define subgroups of women with LN- breast cancer who are at high risk for recurrence. However, these criteria have low accuracy for predicting disease progression and clinical outcome. Such uncertainty can result in inadequate treatment and disease recurrence for some patients and unnecessary treatment with a risk of serious side effects for others. Genetic profiling of tumors allows breast cancers to be classified based on their expression of specific genes that are related to the clinical behavior of the disease. Knowing if a patient's tumor expresses genes associated with disease recurrence can help in determining the appropriate treatment.

Oncotype DX™ is a diagnostic assay that quantifies the likelihood of breast cancer recurrence in women with newly diagnosed, early-stage, LN-, estrogen receptor positive (ER+) breast cancer. Data from the Oncotype DX assay are also used to estimate the potential benefit from chemotherapy. For this test, tumor tissue is excised surgically and sent to a pathology lab where it is fixed in formalin and embedded in paraffin. Micro sections are then cut from the paraffin block and placed in the provided Oncotype tubes. At Genomic Health, tissue RNA is extracted, purified, and analyzed for the expression of 21 genes using real time RT-PCR (reverse-transcriptase polymerase chain reaction). The results are provided as a Recurrence Score™ (RS) that ranges from 0 to 100. Patients are grouped into low-, intermediate- and high-risk categories with higher scores corresponding to higher risk. The physician can use this information along with other data to make treatment decisions.

### *National Comprehensive Cancer Network Statement (2008)*

The National Comprehensive Cancer Network (NCCN) discusses the use of gene expression profiling in the management of breast cancer patients and proposes that this technology will play an important role as a prognostic tool in the future. NCCN states "While many of the DNA microarray technologies are able to stratify patients into prognostic and/or predictive subsets on retrospective analysis, the gene subsets appear to differ from study to study, and prospective clinical trials testing the utility of these techniques have yet to be reported." Pending the results of the TAILORx and MINDACT clinical trials, the NCCN Panel considers Oncotype DX as an option for evaluating "primary tumors characterized as 0.6–1.0 cm with unfavorable features or > 1 cm and node-negative, hormone-receptor positive and HER2-negative. In this circumstance, the recurrence score may assist in estimating the likelihood of recurrence and benefit from chemotherapy." They stress that the recurrence score should be used "for decision making only in the context of other elements of risk stratification."

### *Breast Cancer Staging*

Breast cancer staging is used to determine the extent of the disease upon diagnosis. The stage of the disease is important to develop an appropriate treatment plan and determine the prognosis (expected outcome of the disease). Physical examination, imaging tests (e.g., mammogram, ultrasound), and pathology results following biopsy or other surgery are used to stage breast cancer.

The tumor, node, metastasis (TNM) system classifies cancer by tumor size (T), the degree of regional spread or lymph node involvement (N), and distant metastasis (M). Using this system, breast cancer is assigned a stage from I to IV.

### **Stage 0**

Stage 0 breast cancer sometimes is considered a pre-cancerous condition. Ductal carcinoma in situ (DCIS) is an example of stage 0 breast cancer. In DCIS, cancer cells are located within a milk duct, but have not invaded breast tissue or spread to lymph nodes or distant sites. Other types of breast cancer that may be classified as stage 0 include lobular carcinoma in situ (LCIS) and Paget disease of the nipple.

### **Stage I**

In stage I breast cancer, the tumor is 2 cm or less in diameter (T1) and cancer cells have not spread to lymph nodes (N0) or to distant sites (M0).

### **Stage II**

Stage II breast cancer is classified as stage IIA or stage IIB. A stage IIA classification involves the following:

- no tumor is located in the breast (T0), but cancer cells are found in 1–3 axillary (under the arm) lymph nodes (N1) and have not spread to distant sites (M0); or
- tumor is less than 2 cm in diameter (T1) and cancer cells have spread to 1–3 axillary lymph nodes (N1), but not to distant sites (M0); or
- tumor is larger than 2 cm and less than 5 cm in diameter (T2) and cancer cells have not spread to axillary nodes (N0) or to distant sites (M0).

Stage IIB classification of breast cancer involves the following:

- tumor is larger than 2 cm and less than 5 cm in diameter (T2) and cancer cells have spread to 1–3 axillary lymph nodes (N1), but not to distant sites (M0); or
- tumor is larger than 5 cm and does not grow into the chest wall (T3) and cancer cells have not spread to lymph nodes (N0) or to distant sites (M0).

Breast cancer also is classified as stage IIB when sentinel node biopsy, but not imaging tests or clinical examination, shows that cancer cells have spread to internal mammary lymph nodes.

### **Stage III**

Classifications for stage III breast cancer include stage IIIA, stage IIIB, and stage IIIC. Stage IIIA involves the following:

- tumor is less than 5 cm in diameter (T0–T2) and cancer cells have spread to 4 to 9 axillary lymph nodes (N2), but not to distant sites (M0); or
- tumor is larger than 5 cm (T3) and cancer cells have spread to 1 to 9 axillary nodes (N0–N2) or to internal mammary nodes, but not to distant sites (M0).

In stage IIIB breast cancer, the tumor has grown into the chest wall or the skin (T4) and cancer cells may have spread to as many as 9 axillary nodes (N0–N2), but not to distant sites (M0).

Stage IIIC breast cancer involves a tumor of any size (T0–T4) and cancer cells that have spread to 10 or more axillary lymph nodes, or to 1 or more other regional lymph nodes, or to internal mammary lymph nodes (enlarging these nodes) on the same side as the tumor (N3), but not to distant sites (M0). Inflammatory breast cancer also is classified as stage III, unless it has spread to a distant site.

#### **Stage IV**

Stage IV breast cancer is a tumor of any size (T0-T4) and cancer cells that may have spread to nearby lymph nodes (N0-N3) and have spread to a distant site (M1). Common sites of metastasis include the bones, liver, lungs, brain, and distant lymph nodes.

### **POSITION STATEMENT**

The genetic assay Oncotype DX™ **is considered medically necessary** to assess the need for adjuvant chemotherapy in women with recently diagnosed breast cancer when ALL of the following criteria are met:

- Breast tumor is stage 1 or stage 2; **AND**,
- Breast tumor is Estrogen-Receptor Positive; **AND**,
- Breast tumor is HER2-receptor negative; **AND**,
- There is no evidence of metastatic breast cancer, and the member is axillary-node negative; **AND**,
- The member is a candidate for possible adjuvant chemotherapy (i.e., chemotherapy is not precluded due to other factors), and testing is being done specifically to guide the decision as to whether or not adjuvant chemotherapy will be used.

Oncotype DX™ **is considered experimental and investigational and NOT a covered benefit** for any other clinical evaluation.

All other assays of genetic expression in tumor tissue (e.g., Breast Cancer Gene Expression Ratio, MammaPrint®, Rotterdam Signature 76-Panel) **are considered experimental, investigational and clinically unproven.**

### **CODING**

**CPT®\* Code** - Covered when ALL of the above criteria are met.

**84999** Unlisted Chemistry Procedure

**ICD-9-CM Procedure Codes** - No applicable codes

**HCPCS Level II Code**

**S3854\*** Gene expression profiling panel for use in the management of breast cancer treatment  
\*S- Codes are **NON COVERED FOR MEDICARE – Refer to HCPCS Level II Temporary National Codes**

**ICD-9-CM Diagnosis Codes** – Covered when ALL of the above criteria are met.

- 174.0** Malignant neoplasm of female breast, nipple and areola
- 174.1** Malignant neoplasm of female breast, central portion
- 174.2** Malignant neoplasm of female breast, upper-inner quadrant
- 174.3** Malignant neoplasm of female breast, lower-inner quadrant
- 174.4** Malignant neoplasm of female breast, upper-outer quadrant

- 174.5** Malignant neoplasm of female breast, lower-outer quadrant
- 174.6** Malignant neoplasm of female breast, axillary tail
- 174.8** Malignant neoplasm of female breast, other specified site(s)
- 174.9** Malignant neoplasm of female breast, unspecified site(s)
- V86.0** Estrogen Receptor Positive Status (ER+)

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

## REFERENCES

### Peer Reviewed

1. Hayes Brief, Technology at a Glance. Oncotype Dx™ (Genomic Health Inc.) Genetic Assay for Breast Cancer. Revised October 12, 2007.
2. Hayes Outlook. MammaPrint (70-gene panel/microarray, “Amsterdam signature”) for predicting risk of distal recurrence in patients with early-stage breast cancer. Feb. 7, 2007.
3. Hayes Outlook. 76-gene signature (“Rotterdam signature”) for providing prognostic information to determine the risk of distant disease recurrence in patients with breast cancer. Jan 19, 2007.

### Government Agencies, Professional and Medical Organizations

1. BlueCross BlueShield Association Technology Assessment. Gene Expression Profiling of Breast Cancer to Select Women for Adjuvant Chemotherapy. Volume 22, No. 13. November, 2007.
2. Centers for Medicare and Medicaid Services Local Coverage Determination for Oncotype DX Test-Breast Cancer Prognosis (L27916). June 12, 2008.
3. National Cancer Institute. Molecular test can predict both the risk of breast cancer recurrence and who will benefit from chemotherapy. U.S. National Institutes of Health. Dec 10, 2004.
4. National Comprehensive Cancer Network (NCCN). Breast cancer screening and diagnosis guidelines. 2007.

## HISTORY AND REVISIONS

Date	Action
12/1/2011	<ul style="list-style-type: none"><li>• New template design approved by MPC.</li></ul>
2/26/2011	<ul style="list-style-type: none"><li>• Approved by MPC.</li></ul>