

# MEDICAL POLICY



<b>SUBJECT: GENETIC ASSAY OF TUMOR TISSUE TO DETERMINE PROGNOSIS OF BREAST CANCER (OncotypeDX™, MammaPrint®)</b> <b>POLICY NUMBER: 2.02.27</b> <b>CATEGORY: Laboratory Test</b>	<b>EFFECTIVE DATE: 04/21/05</b> <b>REVISED DATE: 04/20/06, 08/16/07, 10/23/08, 10/29/09, 12/16/10, 11/17/11, 11/15/12, 2/20/14, 01/22/15, 02/18/16, 03/16/17, 01/18/18</b> <b>(DELETED DATE: 11/21/13-2/20/14)</b> <b>PAGE: 1 OF: 9</b>
<ul style="list-style-type: none"><li>• <i>If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.</i></li><li>• <i>If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.</i></li><li>• <i>If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.</i></li></ul>	

## **POLICY STATEMENT:**

- I. Based upon our criteria and review of the peer reviewed literature, the use of the OncotypeDX™ assay has been medically proven to be effective and is considered **medically appropriate** to guide the decision about the need for adjuvant chemotherapy in women with newly diagnosed breast cancer when all of the following criteria are met:
  - A. Breast cancer is unilateral, non-fixed (not adherent to the chest wall); and
  - B. Breast cancer is hormone receptor positive (ER positive or PR positive); and
  - C. Breast cancer is HER2 negative; and
  - D. Tumor size is greater than 0.5 and up to - 1 cm with moderate/poor differentiation or unfavorable features OR tumor size is greater than 1 cm (*refer to Policy Guidelines IV and V*); and
  - E. Tumor is Stage 1 or Stage 2; and
  - F. Breast cancer with 3 or less positive axillary nodes; and
  - G. There is no evidence of distant metastasis; and
  - H. The test result will determine the decision whether to treat the patient with adjuvant chemotherapy AND when the affirmative decision to treat with adjuvant endocrine therapy (e.g., tamoxifen or aromatase inhibitors) has been made; and
  - I. Chemotherapy is not precluded due to other factors; and
  - J. When ordered within 6 months after diagnosis.
- II. Based upon our criteria and review of the peer reviewed literature, all other uses of OncotypeDX™ have not been proven to improve health outcomes and are considered **investigational**.
- III. Based upon our criteria and review of the peer reviewed literature, all other gene expression profiling assays other than OncotypeDX™ have not been proven to improve health outcomes and are considered **investigational** to select women with early stage breast cancer for adjuvant chemotherapy. These assays include but are not limited to:
  - A. The MammaPrint® 70-gene panel;
  - B. Mammostat™;
  - C. Breast Cancer Index<sup>SM</sup> [bioTheranostics, Inc];
  - D. NexCourse® Breast IHC4;
  - E. BreastPRS™;
  - F. Prosigna™; and
  - G. EndoPredict™.
- IV. Based upon our criteria and review of the peer reviewed literature, the use of gene expression assays to molecularly subclassify breast cancer (e.g., Blueprint®) is considered **investigational**.
- V. Based upon our criteria and review of the peer reviewed literature, the use of gene expression assays for quantitative assessment of ER, PR, and HER2 overexpression (e.g., TargetPrint®) is considered **investigational**.

*Refer to Corporate Medical Policy #2.02.30 regarding Genotypic Analysis of Drug Metabolism.*

*Refer to Corporate Medical Policy #11.01.03 regarding Experimental and Investigational Services.*

*Refer to Corporate Medical Policy #11.01.10 regarding Clinical Trials.*

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**POLICY GUIDELINES:**

- I. Assays of genetic expression in tumor tissue are specialized tests that will likely be performed at a limited number of reference laboratories.
- II. Laboratories performing clinical tests must be certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).
- III. The 21-gene RT-pcr assay Oncotype DX should only be ordered after surgery and subsequent pathology examination of the tumor have been completed. The test should be ordered in the context of a physician-patient discussion regarding risk preferences and when the test result will aid the patient in making decisions regarding chemotherapy.
- IV. Unfavorable features that may prompt testing in tumors from 0.6 to 1 cm in size include the following: angiolymphatic invasion, high histologic grade, or high nuclear grade.
- V. Per the National Cancer Institute, risk categories for women with node-negative breast cancer are defined as:
  - A. Low Risk: Tumor size less than 1 cm, and estrogen receptor (ER) or progesterone receptor (PR) status positive, and Tumor Grade of grade 1.
  - B. Intermediate Risk: Tumor size 1-2 cm, ER or PR status positive, Tumor Grade of grade 1-2.
  - C. High risk: Tumor size greater than 2 cm, or ER or PR status negative, or Tumor Grade of grade 2-3.
- VI. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

**DESCRIPTION:**

Prognosis in breast cancer is based on patient age, tumor size, histology, status of the axillary lymph nodes, histologic type, and hormone receptor status. However, patients with the same set of risk factors can have markedly different prognoses. For example, not all patients with larger breast primaries or positive axillary lymph nodes are destined to progress to metastatic disease, and yet adjuvant chemotherapy is routinely recommended in all of these patients. A set of more sensitive and specific risk factors would improve patient selection criteria for adjuvant therapy and other aspects of the treatment of breast cancer.

There has been interest in examining gene expression in tumor tissue as a prognostic factor. For example, RNA can be isolated from tumor tissue, used to generate complementary RNA, which is then labeled and allowed to hybridize to microarrays that can contain up to 25,000 human genes. Positive results are detected by fluorescent intensities. Patterns of genetic expression can then be compared to outcome databases to identify specific patterns associated with prognosis. Gene expression panels, or signatures, are an example of this technology.

Five gene expression stage breast cancer are commercially available in the U.S.: OncotypeDX™ (the 21-gene panel), and the 70-gene panel MammaPrint® (also referred to as the “Amsterdam signature”). Other gene panels include Mammostrat™ (Clariant Diagnostic Services) and the Breast Cancer Index Test (bioTheranostics, Inc).

*OncotypeDX™ assay* (21-gene panel) uses a Recurrence Score™ calculated by a prespecified algorithm, proposes to assess the likelihood of distant recurrence in women with stage I or II, node-negative, estrogen receptor-positive breast cancer treated with tamoxifen. Gene expression profiles from a select panel of 21 genes in the patient’s tumor tissue are analyzed using RT-PCR and an algorithm is used to calculate a Recurrence Score™ that categorizes women as low risk (RS 0-<18), intermediate risk (RS 18-<31) or high risk (RS 31-100).

*Breast Cancer Index test (bioTheranostics, Inc)* is based on the ratio of the expression of two genes: the homeobox gene-B13 (HOXB13) and the interleukin-17B receptor gene (IL17BR). In breast cancers that are more likely to recur, the HOXB13 gene tends to be over-expressed, while the IL-17BR gene tends to be under-expressed.

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*MammaPrint® 70-gene panel*, sometimes referred to as the “*Amsterdam signature*.” uses a customized, manufactured microarray. The gene signature identifies risk classification as high or low risk.

*BluePrint®* is an 80-gene expression assay that classifies breast cancer into basal type, luminal type or HER2-type. The test is marketed as an additional stratifier into a molecular subtype after risk assessment with MammaPrint®.

*TargetPrint®* is a microarray-based gene expression test that offers a quantitative assessment of ER, PR, and HER2 overexpression in breast cancer. The test is marketed to be used in conjunction with MammaPrint® and BluePrint®.

*Endopredict®* (EPclin) analyzes RNA expression of 8 target genes, 3 normalization genes, and 1 control gene, creating a 12-gene molecular score, which is then combined with clinical features of the tumor (tumor size and nodal status) to predict the 10-year distant recurrence (DR) rate. This information may be used by treating physicians to guide therapy decisions by identifying which patients have sufficiently low risk of DR and may forgo chemotherapy, and which patients are at high risk for DR and may need adjuvant chemotherapy in addition to endocrine therapy.

The *Prosigna* Breast Cancer Prognostic Gene Signature Assay is an in vitro diagnostic assay which is performed on the NanoString nCounter® Dx Analysis System using FFPE breast tumor tissue previously diagnosed as invasive breast carcinoma. This qualitative assay utilizes gene expression data, weighted together with clinical variables to generate a risk category and numerical score, to assess a patient’s risk of distant recurrence of disease. The Prosigna Breast Cancer Prognostic Gene Signature Assay is indicated in female breast cancer patients who have undergone surgery in conjunction with locoregional treatment consistent with standard of care.

**RATIONALE:**

In February 2005, a BCBS Association TEC Assessment concluded that gene expression profiling for managing breast cancer treatment did not meet TEC criteria. The TEC Assessment summarized the evidence for 4 different gene expression profiling assays, in various stages of development, that are intended for eventual use in identifying those patients at low risk of recurrence for whom adjuvant chemotherapy can be avoided. These were the 21-gene RT-pcr Oncotype DX™ assay (Genomic Health), the 70-gene MammaPrint® (Agendia; also referred to as the “Amsterdam signature”), the 76-gene “Rotterdam signature” (Veridex), and a 41-gene signature reported by Ahr et al. The TEC Assessment concluded that because published evidence supporting clinical utility was not available, the evidence for all of the gene expression panels was insufficient to permit conclusions.

In 2008, the original BCBS Association TEC Assessment was updated and limited to evaluation of the 3 gene expression profiles commercially available in the United States (Oncotype DX™, MammaPrint®, and the Breast Cancer Gene Expression Ratio). The objective of the updated Assessment was to determine whether, compared to conventional risk assessment tools, the use of gene expression profiling improves outcomes when used to decide if risk of recurrence is low enough to forego adjuvant chemotherapy for early-stage breast cancer. The evidence review is summarized below.

*Oncotype DX™* (Genomic Health, Inc.). Oncotype DX™ is available only from the Clinical Laboratory Improvement Amendments (CLIA)-licensed Genomic Health laboratory as a laboratory-developed service. The test has not been cleared by the U.S. Food and Drug Administration (FDA); to date, FDA clearance is not required, although this may change if and when the FDA draft In Vitro Diagnostic Multivariate Index Assay (IVDMIA) guidelines are finalized and published. Genomic Health indications for the test are newly diagnosed breast cancer patients with stage I or II disease that is node negative and estrogen receptor positive, and who will be treated with tamoxifen.

Results from the Oncotype DX™ 21-gene expression profile are combined into a recurrence score (RS). Tissue sampling, rather than technical performance of the assay, is likely to be the greatest source of variability in results. The Oncotype DX™ assay was validated in studies using archived tumor samples from subsets of patients enrolled in already completed randomized controlled trials of early breast cancer treatment.

Validation and supportive studies delineating the association between RS and recurrence risk indicate strong, independent associations between Oncotype DX™ RS results and distant disease recurrence or death from breast cancer. In secondary analyses of the Paik et al data, patient risk levels were individually classified by conventional risk classifiers, then re-classified by Oncotype DX™. Oncotype DX™ adds additional risk information to the conventional

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clinical classification of individual high-risk patients, and identifies a subset of patients who would otherwise be recommended for chemotherapy but who are actually at lower risk of recurrence (average 7%–9% risk at 10 years; upper 95% CI limits, 11%–15%). Thus, a woman who prefers to avoid the toxicity and inconvenience of chemotherapy and whose Oncotype DX™ RS value shows that she is at very low risk of recurrence might reasonably decline chemotherapy. The lower the RS value, the greater the confidence the woman can have that chemotherapy will not provide net benefit; outcomes are improved by avoiding chemotherapy toxicity.

An additional study, (Paik, et al. 2006) in which samples from a randomized controlled trial of ER-positive, node-negative breast cancer patients treated with tamoxifen versus tamoxifen plus chemotherapy were tested by Oncotype DX™, provides supportive evidence. RS high-risk patients derived clear benefit from chemotherapy, whereas the average benefit for other patients was statistically not significant, although the confidence intervals were wide and included the possibility of a small benefit.

The 2008 Assessment concluded that the 21-gene RT-pcr assay Oncotype DX™ meets criteria for women similar to those in the validation studies. Patients in the validation studies were younger than 70 years of age (or had a life expectancy greater than 10 years), had unilateral, non-fixed, estrogen-receptor (ER) positive, node-negative (by full axillary dissection) carcinomas and were treated with surgery (mastectomy or lumpectomy), radiation therapy, and tamoxifen. Most (92%) patients were negative for HER-2.

Because clinical care for breast cancer patients has evolved since the original trials from which archived samples were acquired for assay validation, differences in evaluation and treatment regimens were considered. It was concluded that the 21-gene Oncotype DX™ meets the TEC criteria for the following women with node-negative breast cancer:

- I. Those receiving aromatase inhibitor (AI)-based hormonal therapy instead of tamoxifen therapy. AI-based therapy would likely reduce recurrence rates for all RS risk groups. Thus, if a patient declined chemotherapy today on the basis of a low-risk RS (risk categories defined by outcomes with tamoxifen treatment), the even lower risk associated with AI treatment would not change that decision.
- II. Those receiving anthracycline-based chemotherapy instead of CMF. The type of chemotherapy does not change the interpretation of the Oncotype DX™ risk estimate. In addition, a recent meta-analysis indicates that anthracyclines do not improve disease-free or overall survival in women with early, HER2-negative breast cancer, and therefore may not be prescribed in this population.
- III. Studies have shown that for women with ER+, node negative disease and low recurrence scores there is little or no benefit from a variety of chemotherapy regimens for distant recurrence, overall survival, and breast-cancer-specific survival. Recent studies have explored the use of OncotypeDx to predict response to chemotherapy for patients with positive axillary lymph nodes. Albain et al., reported results from a Phase III trial of postmenopausal women with node-positive, ER-positive breast cancer. For those patients with 1-3 positive lymph nodes and a low recurrence score there was no benefit of chemotherapy (cyclophosphamide, doxorubicin and fluorouracil [CAF]). For those patients with more than 3 positive lymph nodes with high recurrence scores (after adjustment for the number of positive lymph nodes), there was an improvement in disease-free survival with chemotherapy. In another clinical trial, Dowsett et al, demonstrated that RS is an independent predictor of distant recurrence in N0 and N+ hormone receptor-positive patients treated with anastrozole.
- IV. Those whose tumors are ER-positive or PR-positive. Only ER-positive women were enrolled in Oncotype DX™ validation studies, whereas current clinical guidelines include either ER or progesterone receptor (PR) positivity in the treatment pathway for hormone receptor-positive women with early breast cancer. Recent studies show that ER-negative, PR-positive patients also tend to benefit from hormonal therapy.

In 2010, a TEC Assessment addressed the use of the 21-gene expression assay (Oncotype DX) in lymph node-positive invasive breast cancer patients for the same indications as in the 2005 and 2008 Assessments. The Assessment concluded that use of the 21-gene expression profile for selecting adjuvant chemotherapy in patients with lymph node-positive breast cancer did not meet the TEC criteria.

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The 2016 National Comprehensive Cancer Network (NCCN) guidelines indicate that Oncotype DX for hormone receptor-positive, HER2-negative early breast cancer patients, may be considered in patients whose tumors are node-negative, hormone-receptor-positive, HER2-negative, and 0.6-1 cm in size with moderate/poor differentiation or unfavorable features OR greater than 1 cm in size to assist in estimating likelihood of recurrence and benefit of chemotherapy. The recurrence score should be used for decision making only in the context of other elements of risk stratification for an individual patient. No recommendations are included in the guideline for MammaPrint®. Results from the MINDACT trial are needed to determine the prognostic value and benefit of MammaPrint® in treating intermediate risk patients with adjuvant chemotherapy.

The 2007 American Society of Clinical Oncology (ASCO) guidelines indicate that “In newly diagnosed patients with node-negative, estrogen-receptor positive breast cancer, the Oncotype DX assay can be used to predict the risk of recurrence in patients treated with tamoxifen.” In contrast, the St. Gallen expert consensus panel “did not accept the molecularly based tools such as Oncotype DX™...as sufficiently established to define risk categories.”

Limitations of the current evidence, such as confirmation of optimal RS cutoff values for tamoxifen-treated and separately for AI-treated patients and recommendations for patients with intermediate RS values, are likely to be answered by the results of the ongoing Trial Assigning Individualized Options for Treatment (Rx), also known as TAILORx.

*Breast Cancer Index test (bioTheranostics, Inc).* The Breast Cancer Index test has both predictive and prognostic information included in the test. The prognostic portion of the test includes an algorithmic combination of the molecular index (MGI) and the HoxB13/IL17BR: estrogen signaling pathway along with the expression of 5 cell cycle genes. The 2008 BCBS Association TEC Assessment reviewed available studies and found insufficient evidence to determine whether the Breast Cancer Index test (formerly known as the Breast Cancer Gene Expression Ratio) is better than conventional risk assessment tools in predicting recurrence. Assay configuration and performance characteristics of the commercially available version of the test have not been published. Recurrence rates of patients classified as low risk in available studies were 17%–25%, likely too high for most patients and physicians to consider forgoing chemotherapy. There are no reclassification studies to directly compare the Breast Cancer Gene Expression Ratio with conventional risk classifiers.

*MammaPrint®.* The 2007 BCBS Association TEC Assessment reviewed available studies and found insufficient evidence to determine whether MammaPrint® is better than conventional risk assessment tools in predicting recurrence. Limited technical performance evaluation of the commercial version of the assay suggests good reproducibility. Recurrence rates of patients classified as low risk in available studies were 15%–25%, likely too high for most patients and physicians to consider forgoing chemotherapy. There are no reclassification studies; receiver operating characteristic (ROC) analysis suggests only a small improvement with MammaPrint® classification compared to a conventional classifier. On 2/6/07 the FDA approved MammaPrint® (Agendia, The Netherlands) genetic test. This is the first genetic test to assess breast cancer recurrence risk that is approved by the FDA.

*Blueprint® and TargetPrint®:* The 80-gene expression assay Blueprint® discriminates among 3 breast cancer molecular subtypes, and TargetPrint® is a method to measure ER, PR, and HER2 as an alternative to immunohistochemistry and FISH. Clinical utility of Blueprint® is unknown, as it is unclear how this test will add to treatment decision making using currently available, accepted methods (e.g., clinical and pathologic parameters). The incremental benefit of using TargetPrint® as an alternative to current standard methods of measuring ER, PR, and HER2 has not been demonstrated, nor is it included in recommendations for testing issued by the American Society of Clinical Oncology (ASCO) and the College of American Pathologists.

*Mammostrat™.* Mammostrat™ is an IHC test intended to evaluate risk of breast cancer recurrence in postmenopausal, node negative, estrogen receptor-positive breast cancer patients who will receive hormonal therapy and are considering adjuvant chemotherapy. The test employs 5 monoclonal antibodies to detect gene expression of proteins involved in various aspects of cell proliferation and differentiation and a proprietary diagnostic algorithm to classify patients into high-, moderate-, or low-risk categories. One study reports the development of the assay but provides no information on technical performance (analytic validity). In an independent cohort, a multivariable model predicted 50%, 70%, and 87%

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5-year disease-free survival for patients classified as high, moderate, and low prognostic risk, respectively, by the test results (p=0.0008). There are no published reclassification studies of comparison with conventional risk classifiers. Neither the NCCN, ASCO, nor St. Gallen guidelines support any indications for the use of MammaPrint, Breast Cancer Index<sup>SM</sup>, or Mammostrat™.

**CODES:**      Number                      Description

*Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*

**CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.**

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

<b><u>CPT:</u></b>	81519	Oncology (breast), MRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score
	81520	Oncology (breast), MRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score (Prosignia™) (effective 1/1/2018)
	81521	Oncology (breast), MRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis (MammaPrint®) (effective 1/1/2018)

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<b><u>HCPCS:</u></b>	S3854 (E/I)	Gene expression profiling panel for use in the management of breast cancer treatment
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<b><u>ICD10:</u></b>	C50.011-C50.019	Malignant neoplasm of nipple and areola, female (code range)
	C50.111-C50.119	Malignant neoplasm of central portion of breast, female (code range)
	C50.211-C50.219	Malignant neoplasm of upper-inner quadrant of breast, female (code range)
	C50.311-C50.319	Malignant neoplasm of lower-inner quadrant of breast, female (code range)
	C50.411-C50.419	Malignant neoplasm of upper-outer quadrant of breast, female (code range)
	C50.511-C50.519	Malignant neoplasm of lower-outer quadrant of breast, female (code range)
	C50.611-C50.619	Malignant neoplasm of axillary tail of breast, female (code range)
	C50.811-C50.819	Malignant neoplasm of overlapping sites of breast, female (code range)
	C50.911-C50.919	Malignant neoplasm of breast of unspecified site, female (code range)
	C79.81	Secondary malignant neoplasm of breast
	C79.89-C79.9	Secondary malignant neoplasm of other specified sites (code range)
	D05.00-D05.92	Carcinoma in situ of breast (code range)
	D48.60-D48.62	Neoplasm of uncertain behavior of breast (code range)
	D49.3	Neoplasm of unspecified behavior of breast

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<p><b>SUBJECT: GENETIC ASSAY OF TUMOR TISSUE TO DETERMINE PROGNOSIS OF BREAST CANCER (OncotypeDX™, MammaPrint®)</b></p> <p><b>POLICY NUMBER: 2.02.27</b></p> <p><b>CATEGORY: Laboratory Test</b></p>	<p><b>EFFECTIVE DATE: 04/21/05</b></p> <p><b>REVISED DATE: 04/20/06, 08/16/07, 10/23/08, 10/29/09, 12/16/10, 11/17/11, 11/15/12, 2/20/14, 01/22/15, 02/18/16, 03/16/17, 01/18/18</b></p> <p><b>(DELETED DATE: 11/21/13-2/20/14)</b></p> <p><b>PAGE: 8 OF: 9</b></p>
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**KEY WORDS:**

Breast cancer gene expression ratio, Blueprint®, MammaPrint, Mammostrat™, Oncotype DX, Targetprint®, 70-gene profile, Rotterdam signature, 21-gene panel, 70-gene panel, Prosigna

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## CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

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There is currently no National Coverage Determination (NCD) or Local Coverage Determination (LCD) for genetic assay of tumor tissue to determine prognosis of breast cancer. However, the Medicare Part-B carrier for California, Noridian Healthcare Solutions, LLC, established a favorable Local Coverage Determination (LCD) for the Breast Cancer Index<sup>SM</sup> Genetic Assay. This covers most of Medicare beneficiaries in all 50 states since the bioTheranostics reference laboratory based in San Diego, California, is within the sole jurisdiction of NHIC for purposes of Part B coverage. Please refer to: [https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36314&ver=11&CtrctrSelected=363\\*1&Ctrctr=363&s=6&DocType=Active&bc=AggAAAQIAAAAA%3d%3d&](https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36314&ver=11&CtrctrSelected=363*1&Ctrctr=363&s=6&DocType=Active&bc=AggAAAQIAAAAA%3d%3d&)

There is currently no National Coverage Determination (NCD) or Local Coverage Determination (LCD) for genetic assay of tumor tissue to determine prognosis of breast cancer. However, the Medicare Part-B carrier for Washington, Noridian Healthcare Solutions, LLC, established a favorable Local Coverage Determination (LCD) for the Prosignia<sup>SM</sup> Genetic Assay. This covers most of Medicare beneficiaries in all 50 states since the NanoString Technologies, Inc reference laboratory based in San Diego, California, is within the sole jurisdiction of NHIC for purposes of Part B coverage. Please refer to: [https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36386&ContrId=358&ver=5&ContrVer=1&CtrctrSelected=358\\*1&Ctrctr=358&s=56&DocType=Active&bc=AggAAAQAAAAAA%3d%3d&](https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36386&ContrId=358&ver=5&ContrVer=1&CtrctrSelected=358*1&Ctrctr=358&s=56&DocType=Active&bc=AggAAAQAAAAAA%3d%3d&)