



Medical Policy Manual

Approved Revision: Do Not Implement Until 12/31/26

Breast Cancer Gene Expression Assays

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DESCRIPTION

Laboratory tests have been developed to detect the expression of different genes in breast tumor tissue and combine the results into a prediction of distant recurrence risk (return of detectable cancer in another part of the body) for individuals with early-stage breast cancer. Test results may help determine whether to include adjuvant chemotherapy in post-surgical management of breast cancer. In addition to guiding treatment decisions related to chemotherapy, Breast Cancer index™ has been validated to predict late distant recurrence risk and endocrine responsiveness when considering extension of endocrine therapy.

Most individuals with newly diagnosed, early-stage or nonmetastatic breast cancer are disease-free after initial local and regional treatment; however, almost a third of women develop metastasis by the 4th year follow-up.

Examples of Gene Expression Assays for Breast Cancer:

Test	Description
Breast Cancer Index™	6-11 gene predictor for risk of late recurrence; Predictive of benefit of extended adjuvant endocrine therapy
EndoPredict®	12-gene molecular score for early and late recurrence
MammaPrint®	70 gene analysis; provides low - high risk classification for prognosis determination
Oncotype DX® for Breast Cancer	21-gene assay; Recurrence Score® of 0 - 100 provides prognosis determination
Prosigna® (PAM 50)	Digital analysis system based on prediction of 50 gene microarray; giving a numerical value of 0 - 100 that correlates with the probability of recurrence.

POLICY

- Breast cancer gene expression assay is considered **medically necessary** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Breast cancer gene expression assay is considered **investigational** for other indications including, but not limited to, the following:
 - When performed using InsightTNBCType®

MEDICAL APPROPRIATENESS

- Breast cancer gene expression assay is considered **medically necessary** if **ANY ONE** of the following are met:
 - Test results will guide decision-making regarding adjuvant chemotherapy and **ALL** of the following:
 - Newly diagnosed carcinoma of breast
 - Age and date of diagnosis**
 - Primary, invasive breast cancer



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- Human epidermal growth factor receptor 2 (HER2) negative
- Indicated when **ANY ONE** of the following tests is used:
 - MammaPrint® when **ALL** of the following are met:
 - Female breast cancer
 - Tumor size > 0.5 cm (5mm) in greatest dimension (T1b-T3)
 - Estrogen receptor positive (ER+)
 - Lymph node status is **ANY ONE** of the following:
 - No regional lymph node metastasis (pN0)
 - Involvement of 1-3 positive ipsilateral axillary lymph nodes
 - Oncotype DX® when **ALL** of the following are met:
 - Male or Female breast cancer
 - Tumor size > 0.5 cm (5mm) in greatest dimension (T1b-T3)
 - Estrogen receptor positive (ER+)
 - Lymph node status is **ANY ONE** of the following:
 - No regional lymph node metastasis (pN0)
 - Involvement of 1-3 positive ipsilateral axillary lymph nodes
 - EndoPredict® when **ALL** of the following are met:
 - Female breast cancer
 - Unilateral tumor
 - Tumor size > 0.5 cm (5mm) in greatest dimension (T1b-T3)
 - Hormone receptor positive (ER+ or PR+)
 - Lymph node status is **ANY ONE** of the following:
 - No regional lymph node metastasis (pN0)
 - Involvement of 1-3 positive ipsilateral axillary lymph nodes
 - Breast Cancer Index™ when **ALL** of the following are met:
 - Female breast cancer
 - Unilateral tumor
 - Tumor size > 0.5cm (5mm) in greatest dimension (T1b-T3)
 - Hormone receptor positive (ER+ or PR+)
 - Lymph node status is **ANY ONE** of the following:
 - Individual has no regional lymph node metastasis (pN0)
 - Micrometastases (pN1mi, malignant cells in regional lymph node(s) not greater than 2.0mm)
 - Prosigna® when **ALL** of the following are met:
 - Female breast cancer
 - Tumor size equal to or greater than 0.4 cm (4mm) in greatest dimension (T1b-T3)
 - Hormone receptor positive (ER+/PR+)
 - No regional lymph node metastasis
- Test results will predict benefit of extended endocrine therapy beyond **four** years when **ALL** of the following are met:
 - Test performed using Breast Cancer Index™
 - Female breast cancer
 - **Age and date of diagnosis**
 - Unilateral tumor
 - Tumor size > 0.5cm (5mm) in greatest dimension (T1b-T3)
 - Hormone receptor positive (ER+ or PR+)
 - Lymph node status is 0 – 3 positive nodes
- **Blueprint® when ALL of the following are met:**



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- Histologically confirmed invasive breast cancer
- Early-stage breast cancer
- Treatment planning is under consideration
- Results are expected to influence systemic therapy selection
- Testing is being used to further characterize tumor biology beyond standard ER, PR, and HER2 testing
- Results are expected to affect chemotherapy recommendations
- Oncotype DX® Breast Recurrence Score - 21-gene expression assay with prognostic and predictive genomic classifier when **ALL** of the following are met:
 - Newly diagnosed invasive breast cancer
 - ER-positive disease
 - HER2-negative disease
 - Chemotherapy benefit is uncertain
 - Results are expected to influence adjuvant treatment decisions
- Oncotype DX® Breast DCIS Score with gene expression assay designed for ductal carcinoma in situ (DCIS) when **ALL** of the following are met:
 - Histologically confirmed DCIS
 - Breast-conserving treatment is being considered or has been performed
 - Results are expected to influence local treatment planning
 - Results may affect decisions regarding **ANY ONE** of the following:
 - Radiation therapy
 - Surveillance
 - Local recurrence risk assessment

IMPORTANT REMINDERS

- Any specific products referenced in this policy are just examples and are intended for illustrative purposes only. It is not intended to be a recommendation of one product over another and is not intended to represent a complete listing of all products available. These examples are contained in the parenthetical e.g. statement.
- We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits, or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

ADDITIONAL INFORMATION

Tests intended to assess estrogen receptor, progesterone receptor and *HER2* status, such as TargetPrint®, and tests that do not provide a specific recurrence risk are outside the scope of this policy.

SOURCES



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