CLINICAL POLICY AND PROCEDURE MANUAL

Policy Number: PA.018.CC
Last Review Date: 07/09/2024
Effective Date: 08/01/2024

PA.018.CC Gene Expression Testing for Breast Cancer

Summary

About one in eight women will develop breast cancer during their lifetime in the United States. Breast cancer is the second most commonly diagnosed cancer among women behind skin cancer. Breast cancer refers to a malignant tumor in the breast caused by an uncontrolled growth in cells and it is always caused by a genetic abnormality. Leading risk factors include increasing in age and being of the female sex.

If breast cancer is detected, various tests can be performed for additional insight on the rate of growth, likelihood of spreading or return and the potential effectiveness of treatment options. Mutigene tests are one set of tests utilized and they can include:

- **Oncotype DX**: multigene test that predicts whether Stage I or Stage II breast cancer that is estrogen receptor positive and node negative will spread to other parts of the body.
- **MammaPrint**: multigene test that predicts whether Stage I or Stage II breast cancer that is node negative will spread to other parts of the body.
- **Prosigna**: multigene test for post-menopausal women that predicts whether Stage I or Stage II breast cancer that is estrogen receptor positive and node negative will spread to other parts of the body
- **Breast Cancer Index (BCI) (bioTheranostics)**: for non-relapsed, ER+ breast cancer
- **Endopredict (EndoPredict® for Breast Cancer Prognosis)**: considered medically necessary only for women with T1-3, N0-1 breast cancer

If these tests indicate a high chance of spreading, chemotherapy may be given to lower the risk.

Oncotype DX Scores (risk of recurrence)

- 0 < 18: low risk
- 18-31: intermediate risk
- ≥ 31: high risk

Prosigna Scores (risk of recurrence):

- 0-40: low risk
- 41-60: intermediate risk
- 61-100: high risk

Clinical Criteria

County Care considers **gene expression testing** for breast cancer medically necessary for the following indications:

Oncotype DX (Oncotype DX® Breast Recurrence Score) is considered medically necessary ***only for women who meet all the following criteria***:

1. Diagnosed with Stage I or II breast cancer within the previous six months; and
2. Lymph node-negative; and
3. Estrogen receptor (ER) positive tumor; and
4. Her2 negative tumor; and
5. The woman would be a candidate for adjuvant chemotherapy and
6. Member and treating Medical Provider (prior to testing) have discussed the potential results of the Gene expression profiling test and agree to use the results to guide cancer therapy.

MammaPrint® is considered medically necessary ***only for women who meet all of the following criteria***:

1. Diagnosed with stage I or II breast cancer within the previous six months; and
2. Lymph node-negative; and
3. Tumor smaller than 5.0 centimeters; and
4. Estrogen receptor (ER) positive or negative tumor; and
5. Her2 negative tumor; and
6. The woman would be a candidate for adjuvant chemotherapy and
7. Member and treating Medical Provider (prior to testing) have discussed the potential results of the Gene expression profiling test and agree to use the results to guide cancer therapy.

Prosigna (Prosigna® Breast Cancer Prognostic Gene Signature Assay) is considered medically necessary ***only for post-menopausal women who meet all of the following criteria***:

1. Diagnosed with Stage I or II breast cancer within the previous six months; and
2. Lymph node-negative or Stage II with 1-3 positive nodes; and
3. Estrogen receptor (ER) positive tumor; and
4. Her2 negative tumor; and

5. The woman would be a candidate for adjuvant chemotherapy and
6. Member and treating Medical Provider (prior to testing) have discussed the potential results of the Gene expression profiling test and agree to use the results to guide cancer therapy.

Breast Cancer Index (**BCI**) (bioTheranostics) is considered medically necessary only for women who meet all of the following criteria:

1. Member with non-relapsed, ER+ breast cancer,
2. Was lymph node negative,
3. Is completing five years of endocrine therapy,
4. Patient must be eligible for consideration of extended endocrine therapy based on published clinical trial data or practice guidelines,
5. Physician or patient is concerned about continuing anti-hormonal therapy because of documented meaningful toxicity or possible significant patient specific side effects,
6. The test results will be discussed with the patient (including the limitations of the testing method, the risks, and benefits of either continuing or stopping the therapy based on the test, and current cancer management guidelines).

Endopredict (EndoPredict® for Breast Cancer Prognosis) is considered medically necessary only for women with T1-3, N0-1 breast cancer when the following criteria are met:

1. Tumor size greater than 0.5cm (5mm) in greatest dimension (T1b-T3); and
2. Patient is post-menopausal, and
3. Pathology (excisional or biopsy) reveals invasive carcinoma of the breast that is ER-positive, Her2-negative, and
4. Patient is either lymph node-negative or has 1-3 positive lymph nodes, and
5. Patient has no evidence of distant metastasis, and
6. Test result will be used to determine treatment choice between endocrine therapy alone vs. endocrine therapy plus chemotherapy.

Note: The EndoPredict test should not be ordered if a physician does not intend to act upon the test result.

Use of gene expression profiling with EndoPredict, Prosigna Breast Cancer Prognostic Gene Signature Assay, or the Breast Cancer Index (BCI) as a genetic index is used to assist in decisions of extending adjuvant hormonal therapy beyond 5 years of treatment when all of the following criteria are met:

- When all the above stated criteria have been met for each test; and when the Oncotype DX Breast Recurrence Score was the initial gene expression profiling test used, and
- the individual is a candidate for additional cancer therapy.

Limitations

1. **A maximum of one genomic assay per breast tumor is considered medically necessary and therefore second or subsequent genomic assays on the same tumor are not covered**.
2. Gene expression testing for breast cancer will *only be covered if an oncologist orders the test*.
3. Since gene expression assays analyze ribonucleic acid (RNA) and RNA is unstable:
    - Assay samples are to be obtained at the time of tumor excision;
    - Time from excision to fixation should be less than 1 hour (see College of American Pathologists/American Society of Clinical Oncology (CAP/ASCO) protocol; reference below);
    - Formalin fixed paraffin blocks that are greater than six months old should not be tested.
4. **OncotypeDx Breast DCIS Score test** is considered experimental, investigational, or unproven. Gene expression profiling as a technique of managing the treatment of ductal carcinoma in situ (DCIS) (when DCIS is the sole breast cancer histology) is considered not medically necessary under all circumstances.
5. **County Care considers Mammaprint, Oncotype DX, and Prosigna to be experimental/investigational for any other uses, reasons, or tissue type**.

Codes

CPT/HCPCS Codes	
Code	**Description**
0458U	Oncology (breast cancer), S100A8 and S100A9, by enzyme-linked immunosorbent assay (ELISA), tear fluid with age, algorithm reported as a risk score
81518	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy

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
81522	Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes (8 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk score
81523	Oncology (breast), mRNA, next-generation sequencing gene expression profiling of 70 content genes and 31 housekeeping genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk to distant metastasis
81599	Unlisted multianalyte assay with algorithmic analysis
S3854	Gene expression profiling panel for use in the management of breast cancer treatment

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Archived References

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Revision History

Revision	Date
Policy Created	08/2022
Annual Review completed, formatting updates made	09/14/2023
Updated Policy to add procedure code S3854; added Breast Cancer Index and Endopredict under Summary; reordered info under Clinical Criteria	11/28/2023
Annual review completed - Formatting updates to body of policy and Reference	05/16/2024

#4; updated "Last Updated" date in Reference #s 5, 6, 7 and 9; added "Last" to updated date in Reference #19; updated Revision Effective Date and replaced invalid link in Reference #21	
Added newly effective procedure code 0458U	07/09/2024

Disclaimer

CountyCare medical payment and prior authorization policies do not constitute medical advice and are not intended to govern or otherwise influence the practice of medicine. The policies constitute only the reimbursement and coverage guidelines of CountyCare and its affiliated managed care entities. Coverage for services varies for individual members in accordance with the terms and conditions of applicable Certificates of Coverage, Summary Plan Descriptions, or contracts with governing regulatory agencies.

CountyCare reserves the right to review and update the medical payment and prior authorization guidelines in its sole discretion. Notice of such changes, if necessary, shall be provided in accordance with the terms and conditions of provider agreements and any applicable laws or regulations.