# MedStar Health, Inc.
## POLICY AND PROCEDURE MANUAL

Policy Number: PA.018.MH
Last Review Date: 07/27/2021
Effective Date: 11/15/2021

## PA.018.MH – Gene Expression Testing for Breast Cancer

This policy applies to the following lines of business:
- ✓ MedStar Employee (Select)
- ✓ MedStar CareFirst PPO

MedStar Health considers **gene expression testing** for breast cancer medically necessary for the following indications:

**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. The result of the test will guide the decision whether or not to use chemotherapy; and
7. The woman would choose to receive chemotherapy if offered.

**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. The result of the test will guide the decision whether or not to use chemotherapy; and
8. The woman would choose to receive chemotherapy if offered.

**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. The result of the test will guide the decision whether or not to use chemotherapy; and
7. The woman would choose to receive chemotherapy if offered.

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

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, andPathology (excisional or biopsy) reveals invasive carcinoma of the breast that is ER-positive, Her2-negative, and
3. Patient is either lymph node-negative or has 1-3 positive lymph nodes, and
4. Patient has no evidence of distant metastasis, and
5. 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.

**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 the test is ordered by an oncologist*.
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. Evolent Health considers Mammaprint, Oncotype DX, and Prosigna to be **experimental/investigational for any other uses, reasons, or tissue type**.

**Background**

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

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

**Codes:**

| CPT/HCPCS Codes | |
|---|---|
| Code | Description |
| 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 |
| S3854 | Gene expression profiling panel for use in the management of breast cancer treatment |

**References**

1. About Oncotype DX- Illuminating Breast Cancer Recurrence Risk- www.genomichealth.com
2. Azim HA, Jr., Michiels S, Zagouri F, et al. Utility of prognostic genomic tests in breast cancer practice: The IMPAKT 2012 Working Group Consensus Statement. Ann Oncol. 2013 Mar; 24(3):647-654. http://www.ncbi.nlm.nih.gov/pubmed/23337633
3. Badve S. Sentinel Lymph Node Biopsy. Ch. 7. In: Breast Pathology. (Dabbs DJ, ed.). Elsevier/Saunders; Philadelphia. 2012. ISBN. 978-1-4377-0604-8.
4. Barton MK: Researchers Find Discordance between standard human epidermal growth factor receptor 2 (HER2) testing and HER2 status reported on Oncotype DX. CA Cancer J Clin. 2012 Jan 18. doi: 10.3322/caac.21133 https://www.ncbi.nlm.nih.gov/pubmed/22259018

5. Breast Cancer Treatment (PDQ®), Stages of Breast Cancer, National Cancer Institute at the National Institute of Health. Last modified: 04/08/2021. http://www.cancer.gov/cancertopics/pdq/treatment/breast/Patient/page2#Keypoint13
6. Breastcancer.org, MammaPrint Test. Last modified: January 26, 2021. http://www.breastcancer.org/symptoms/testing/types/mammaprint
7. Breastcancer.org, Oncotype DX Test. Last Modified: April 27, 2021. http://www.breastcancer.org/symptoms/testing/types/oncotype_dx
8. Breastcancer.org, Prosigna Breast Cancer Prognostic Gene Signature Assay. Last modified: January 26, 2021. http://www.breastcancer.org/symptoms/testing/types/prosigna
9. Breastcancer.org, U.S. Breast Cancer Statistics. Last modified: February 4, 2021. http://www.breastcancer.org/symptoms/understand_bc/statistics
10. Carlson RW, Allred DC, Anderson BO, et al.: Invasive breast cancer: clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2011;9:136-222 http://www.jnccn.org/content/9/2/136.full.pdf+html?sid=e2e09de5-3097-49b0-a749-298856d07c8a
11. Centers for Medicare and Medicare Services (CMS). Local Coverage Determination (LCD) L36021 - Molecular Diagnostic Tests (MDT) (Contractor: CGS Administrators, LLS). Revision Effective Date: 12/19/2019. https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36021&ver=43&MCDIndexType=6&mcdtypename=Compendia&TAId=94&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=molecular+diagnostic+tests&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAAAgAAAAA&
12. Centers for Medicare and Medicaid Services (CMS). Technology Assessment of Molecular Pathology Testing for the Estimation of Prognosis for Common Cancers. Final May 29, 2014. https://www.cms.gov/medicare-coverage-database/details/technology-assessments-details.aspx?TAId=94&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=molecular+diagnostic+tests&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAABAAAAAAAA%3d%3d&
13. Dvorak L, Dolan M, Fink J, et al. Correlation between HER2 determined by fluorescence in situ hybridization and reverse transcription-polymerase chain reaction of the Oncotype DX test. Appl Immunohistochem Mol Morphol. 2013 May; 21:196-199. http://www.ncbi.nlm.nih.gov/pubmed/22914611
14. EGAPP Working Group (Berg AO, Armstrong K, Botkin J, et al): Recommendations from the EGAPP Working Group: can tumor gene expression profiling improve outcomes in patients with breast cancer?, Genet Med; 2009; 11:66-73 https://www.ncbi.nlm.nih.gov/pubmed/19125125

15. Goncalves R, Bose R:Using multigene tests to select treatment for early-stage breast cancer. J Natl Compr Canc Netw. 2013 Feb; 11(2):174-182 :, http://www.jnccn.org/content/11/2/174.full.pdf+html?sid=e2e09de5-3097-49b0-a749-298856d07c8a
16. Hammond ME, Hayes DF, Allred DC, et al., American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Immunohistochemical Testing of Estrogen and Progesterone Receptors in Breast Cancer. ASCO; 2010. https://pubmed.ncbi.nlm.nih.gov/20404251/
17. Klein ME, Dabbs DJ, Shuai Y, et al. Prediction of the Oncotype DX recurrence score: use of pathology-generated equations derived by linear regression analysis, Mod Pathol 2013 Mar 15. Doi 10.1038/modpathol.2013.36 http://www.ncbi.nlm.nih.gov/pubmed/23503643
18. Markopoulos, C. Overview of the Use of Oncotype DX as an Additional Treatment Decision Tool in Early Breast Cancer. 2013. http://www.medscape.com/viewarticle/779859_1
19. National Institute for Health and Clinical Excellence (NICE). Quality Standard: Breast cancer. Issued: Sept. 2011, Updated: June 2016 https://www.nice.org.uk/guidance/qs12
20. Paik S, Shak S, Tang G, et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. N Engl J Med. 2004;351(27):2817-2826 https://www.ncbi.nlm.nih.gov/pubmed/15591335

**Archived References**

1. Hayes GTE Overview. Breast Cancer Index. Annual Review November 25, 2015. Archived September 11, 2018.

**Disclaimer:**

MedStar Health 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 MedStar Health 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.

MedStar Health 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.