EVH Clinical Guideline 2704.CC for Gene Expression Testing for Breast Cancer

Guideline Number: EVH_CG_2704.CC	Applicable Codes	
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Original Date: October 1, 2022	**Last Revised Date:** November 20, 2025	**Implementation Date:** December 1, 2025

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STATEMENT

General Information

- *It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.*
- *Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines, and state/national recommendations.*
- *The guideline criteria in the following sections were developed utilizing evidence-based and peer-reviewed resources from medical publications and societal organization guidelines as well as from widely accepted standard of care, best practice recommendations.*

INDICATIONS

CountyCare considers **Gene Expression assay testing** medically necessary for the following indications:

CATEGORY A

- To help assess benefits from chemotherapy and endocrine (anti-estrogen) therapy in Stage I and II breast cancer that is estrogen receptor-positive (ER+), progesterone receptor-positive (PgR+), and ERBB2-negative (formally known as human epidermal growth factor receptor 2 negative (HER2-negative).
    - **Oncotype DX® (Oncotype DX® Breast Recurrence Score)** is for women who meet **ALL** the following criteria [1,3]:
        - Diagnosed with Stage I or II breast cancer within the previous six months
        - Lymph node-negative OR lymph-node positive with 1-3 positive nodes in postmenopausal women (not recommended for premenopausal women with 1-3 positive nodes)
        - Tumor < 5.0 cm
        - ER/PgR+ tumor
        - ERBB2-negative or HER2-negative tumor
    - **MammaPrint®** is for women who meet **ALL** of the following criteria [1,2]:
        - Diagnosed with primary breast cancer
        - Postmenopausal or > 50 years old

- ER/PgR+ tumor
- ERBB2-negative or HER2-negative tumor
- Axial nodal staging is pN0 or pN1mi or pN1 (1-3 nodes)
- The patient is a candidate for adjuvant therapy
- The patient is a candidate for adjuvant chemotherapy

- **Prosigna® (Prosigna® Breast Cancer Prognostic Gene Signature Assay)** is 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
  - Lymph node-negative
  - ER/PgR+ tumor
  - ERBB2-negative or HER2-negative tumor
  - The patient is a candidate for adjuvant therapy

CATEGORY B

- Assess benefits of extended (> 5 years and up to 10 years) of adjuvant hormonal (anti-estrogen) therapy [1,3]:
  - **Breast Cancer Index (BCI)** is for women who meet ANY of the following criteria:
    - ER/PgR+ tumor
    - ERBB2-negative or HER2-negative tumor
    - Lymph-node negative OR lymph-node positive with 1-3 positive nodes and treated with 5 years of primary endocrine therapy without evidence of recurrence[1,3]
    - Patient must be eligible for consideration of extended endocrine therapy
  - **EndoPredict (EndoPredict® for Breast Cancer Prognosis)** is for women with T1-3, N0-1 breast cancer when the following criteria are met:
    - Postmenopausal
    - Lymph-node negative or node positive with 1-3 positive nodes
    - ER-positive, HER2-negative, and
    - Patient has no evidence of distant metastasis

LIMITATIONS

- A maximum of one genomic assay in Category A and 5 years later you can have Breast Cancer Index
- A second or subsequent genomic assays Category A on the same tumor are not covered

- The Breast Cancer Index test is typically performed once per patient lifetime, specifically on the original tumor specimen, and is currently limited to individuals assigned female at birth
- The use of Oncotype DX Breast Recurrence Score may be considered medically necessary for all patients, regardless of gender
- The use of other breast cancer prognostic algorithmic tests (i.e., EndoPredict, Prosigna, MammaPrint) in individuals assigned male at birth are considered investigational
- **County Care considers Mammaprint, Oncotype DX, and Prosigna to be experimental/investigational for any other uses, reasons, or tissue type**

CODING AND STANDARDS

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

Code	Description
S3854	Gene expression profiling panel for use in the management of breast cancer treatment

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☐	Commercial
☐	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
November 20, 2025	• This guideline replaces PA.018.CC Gene Expression Testing for Breast Cancer • Editorial changes to match the formatting and layout of the new template, no changes to clinical content

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Administrative Services Medical Policy Committee

Disclaimer

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REFERENCES

1. Andre F, Nofisat Ismaila ;, Allison KH, et al. Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update.; 2022. **https://www.asco.org/breast-cancer-guidelines**
2. Piccart M, van 't Veer LJ, Poncet C, et al. 70-gene signature as an aid for treatment decisions in early breast cancer: updated results of the phase 3 randomised MINDACT trial with an exploratory analysis by age. Lancet Oncol. 2021;22(4):476-488. doi:10.1016/S1470-2045(21)00007-3. **https://pubmed.ncbi.nlm.nih.gov/33721561/**
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