Breast Cancer Prognostic Algorithmic Tests

I. The use of a breast cancer prognostic algorithmic test (i.e., EndoPredict, Prosigna, MammaPrint) is considered **medically necessary** when:

   A. The member is female (sex assigned at birth), **AND**

   B. The member meets at least one of the following:

      1. Postmenopausal status, **OR**

      2. Greater than 50 years of age, **AND**

   C. The member has primary breast cancer that is ductal/NST, lobular, mixed or micropapillary, **AND**

   D. The member's tumor is estrogen receptor-positive, **AND**

   E. The member's tumor is human epidermal growth factor receptor 2 (HER2)-negative, **AND**

   F. The member is considering treatment with adjuvant therapy (e.g., tamoxifen, aromatase inhibitors, immunotherapy), **AND**

   G. The member has had axillary nodal staging and has the following node status:

      1. pN0 (nodes negative pathologically), **OR**

      2. pN1mi or pN1 (1-3 nodes positive pathologically)[1].

II. The use of a breast cancer prognostic algorithmic test (i.e., EndoPredict, Prosigna, MammaPrint) in individuals with 4 or more positive nodes is considered **investigational**.

III. The use of the breast cancer prognostic algorithmic test Prosigna in individuals with 1-3 node positive breast cancer is considered **investigational**.

IV. The use of a breast cancer prognostic algorithmic test (i.e., EndoPredict, Prosigna, MammaPrint) in men (sex assigned at birth) with breast cancer is considered **investigational**.

V. The use of a breast cancer prognostic algorithmic test (i.e., EndoPredict, Prosigna, MammaPrint) is considered **investigational** for all other indications.

[1] Prosigna is indicated for node negative disease, but **not** for disease with 1-3 positive nodes. EndoPredict and Mammaprint are indicated for node negative disease and for disease with 1-3 positive nodes.

RATIONALE AND REFERENCES

Breast Cancer Prognostic Algorithmic Tests

American Society of Clinical Oncology (ASCO)

The 2022 ASCO guideline update for Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer provides guidance for the diagnostic indications for several breast cancer prognostic algorithmic tests, including EndoPredict, MammaPrint, and Prosigna (among others).

Figure 1 (p. 1821) includes an algorithm that acts as a guide for prognostic test choice in women with early-stage invasive breast cancer. In summary, a female patient must have the following in order to recommend EndoPredict, Prosigna, or MammaPrint testing:

- Postmenopausal **OR** older than age 50 years
- Early-stage invasive breast cancer
- Node negative disease,
- HER2 negative tumor
- ER positive tumor

Of note, per the guide, if the patient has 1 to 3 positive node disease then only MammaPrint or EndoPredict may be ordered. The algorithm also shows that there is "Insufficient evidence to recommend a biomarker for use” in women with 4 or more positive nodes (p. 1821).

Andre F, Ismaila N, Allison KH, et al. Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update [published correction appears in J Clin Oncol. 2022 Aug 1;40(22):2514]. J Clin Oncol. 2022;40(16):1816-1837. doi:10.1200/JCO.22.00069

National Comprehensive Cancer Network (NCCN): Breast Cancer (4.2025)

This guideline recommends consideration of other prognostic gene expression assays to help assess risk of recurrence in pre- and postmenopausal patients with either ductal/NST, lobular, mixed, or micropapillary breast cancer that is HR-positive, Her2-negative, pT1-3 and pN0 or pN+. However, these other tests have not been validated to predict response to chemotherapy (p. BINV- 6, BINV-7, BINV-8).

A footnote on page BINV-N 3 of 5 states: “Gene expression assays can provide prognostic and treatment-predictive information that can be used with T,N,M and biomarker information”. These prognostic gene expression assays can provide prognostic information but there is limited evidence for prediction of chemotherapy benefit (p. BINV-N 3 of 5).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

DEFINITIONS

1. **Adjuvant** therapy is a medication (such as chemotherapy or endocrine therapy) given after the surgical removal of a cancerous tumor.
2. **Ductal/NST** is a ductal breast cancer of no special type (NST), meaning the cancer cells have no features that classify them as a specific type of breast cancer when examined by microscope.