PRESBYTERIAN

Medical Policy

Subject: Genetic Testing for Breast Cancer Recurrence and Predictive

Medical Policy #: 33.0

Original Effective Date: 07-31-2019

Status: Reviewed

Last Annual Review Date: 12-11-2024

Disclaimer

Refer to the member's specific benefit plan and Schedule of Benefits to determine coverage. This may not be a benefit on all plans, or the plan may have broader or more limited benefits than those listed in this Medical Policy.

PHS follows CMS LCDs, and other Medicare manuals to provide support for determining coverage. The providers are expected to provide appropriate documentation when requested to support coverage. This policy is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this policy and Medicare source materials, the Medicare source materials will apply.

Coverage Determination

Prior Authorization is not required. Logon to Pres Online to submit a request:
https://ds.phs.org/preslogin/index.jsp

1. **Oncotype-DX:**

   For Medicare, Medicaid and Commercial:

   PHP is following LCA (A55230), MolDX: Oncotype DX® Breast Cancer Assay: Test coverage for patients with the following findings:

   - estrogen-receptor positive, node-negative carcinoma of the breast,
   - estrogen-receptor positive micrometastases of carcinoma of the breast,
     and
   - estrogen-receptor positive breast carcinoma with 1-3 positive nodes

2. **Oncotype DX® for Ductal Carcinoma in Situ (DCIS):**

   For Medicare members only:

   PHP is following CMS LCD (L37199). The Oncotype DX® Breast Cancer for DCIS assay, related article (A57583), is covered when **all** the following clinical conditions are met:

   - Pathology (excisional or core biopsy) reveals ductal carcinoma in situ of the breast (no pathological evidence of invasive disease), **and**
   - FFPE specimen with at least 0.5 mm of DCIS length, **and**
   - Patient is a candidate for and is considering breast conserving surgery alone as well as breast conserving surgery combined with adjuvant radiation therapy, **and**
   - Utilize the test result to determine treatment choice between surgery alone vs. surgery with radiation therapy, **and**
   - Member has not received and is not planning on receiving a mastectomy.

   Non-covered for Medicaid and Commercial:

3. **ENDOPredict® (Myriad Genetics):**

   For Medicare:

   PHP is following CMS MolDX: EndoPredict® Breast Cancer Gene Expression Test, LCD (L37663), related article (A57567). The EndoPredict® assay is reasonable and necessary to assist physicians in the managing early-stage breast cancer.

The assay is covered for women with T1-3, N0-1 breast cancer when **all** the following are met:

- Is post-menopausal, **and**
- Pathology (excisional or biopsy) shows invasive carcinoma of the breast that is Estrogen-Receptor (ER)-positive, Her2-negative, **and**
- Has either lymph node-negative or has 1-3 positive lymph nodes, **and**
- Has no evidence of distant metastasis, **and**
- Result of test 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.

For Medicaid and Commercial:

PHP is following NCCN guidelines when **all** the following are met.

- Breast tumor is HER2 negative; **and**
- Breast tumor is HR positive; **and**
- Node negative (lymph nodes with micrometastases [less than or equal to 2 mm in size] are considered node negative for this policy statement) OR one to three positive lymph nodes (NI); **and**
- Breast tumor size greater than 0.5 cm; **and**
- Medically eligible for adjuvant therapy; **and**
- No distant metastasis.

4. **MammaPrint®:**

For Medicare, Medicaid and Commercial:

PHP is following CMS MolDX: MammaPrint LCA A55175. MammaPrint® is a diagnostic test that analyzes the gene expression profile of FFPE breast cancer tissue samples to assess a patients' risk for distant metastasis. Must meet **all** the following:

- Early-stage breast cancer,
- tumor size <5cm up to 3 positive lymph nodes, **and**
- independent of receptor status.

Note: MolDX expects this test may be performed upon occasion twice per patient lifetime for bilateral disease. Additional testing will be considered on a case-by-case basis.

5. **Prosigna:**

For Medicare:

PHP is following CMS LCD Breast Cancer Assay: Prosigna, (L36811) and (A57560); Biomarkers for Oncology, (L35396).This policy provides limited coverage of the Prosigna breast cancer gene signature assay to patients that meet the following criteria:

Post-menopausal female with **either:**

- Estrogen-Receptor (ER) +, lymph node-negative, stage I or II breast cancer; **or**
- Estrogen-Receptor (ER) **+**, lymph node-positive (1-3 positive nodes), stage II breast cancer.

For **Medicaid, and Commercial:**

PHP follows NCCN, when **all** the following are met.

- Breast tumor is HER2 negative; **and**
- Breast tumor is HR positive; **and**
- Breast tumor size greater than 0.5 cm; **and**
- Medically eligible for adjuvant therapy **and**
- Negative axillary lymph nodes (nonmetastatic) (pN0) or axillary node micrometastasis (pN1mi) no greater than 2.0 mm

6. **Breast Cancer Index (BCI):**

For Medicare:

PHP is following CMS Breast Cancer Index® (BCI) Gene Expression Test LCD (L37913) and the related article LCA (A56335).

Coverage Indications, Limitations, and/or Medical Necessity

This Medicare contractor will provide limited coverage for the Breast Cancer Index® (BCI) gene expression test (Biotheranostics, Inc., San Diego, CA). The BCI test is used by physicians to provide a genomic-based estimate of distant recurrence risk when considering addition of chemotherapy, and/or late distant recurrence risk and endocrine responsiveness when considering extension of endocrine therapy, depending upon when in the continuum of care testing is requested.

The BCI test is covered for postmenopausal women with invasive breast cancer when **all** the following criteria are met:

- Pathology reveals invasive carcinoma of the breast that is estrogen-receptor positive (ER+) and/or progesterone receptor positive (PR+) and Human Epidermal Growth Factor Receptor 2 negative (HER2-); **and**
- Patient has early-stage disease {Tumor, Node, Metastasis (TNM) stage T1-3, pN0-N1, M0}; **and**
- Patient has no evidence of distant breast cancer metastasis (i.eg., non-relapsed); **and**
- Test results will be used in determining treatment management of the patient for chemotherapy and/or endocrine therapy.

For Medicaid and Commercial:
PHP is following NCCN guidelines. Breast Cancer Index (BCI) Risk of Recurrence and Extended Endocrine Benefit Test (CPT code 81518) is considered medically necessary for a woman with early stage T1-T3 breast cancer diagnosed within the last five years when **all** the following criteria are met:

- estrogen receptor (ER) positive, **and**
- human epidermal growth factor receptor 2 (HER2) negative, **and**
- there is no evidence of distant metastasis, **and**
- EITHER of the following:
    - axillary node status is negative (micrometastasis no greater than 2.0 mm)
    - axillary node status is positive (LN+ with 1-3 positive nodes)

  and
- there is no evidence of cancer at the time of testing, **and**
- test results will be used to determine treatment management of the individual for extended endocrine therapy after completion of at least four years of endocrine therapy.

Coding

The coding listed in this medical policy is for reference only. Covered and non-covered codes are within this list.

Generally, the test for Breast Cancer Recurrent Predictive Genetic listed below is covered only once in a lifetime; however, request submitted for consideration will be reviewed on a case-by-case basis.

Test Name	CPT Codes	Breast Cancer Recurrent Predictive Genetic Test Description
OncoType DX®	81519	Oncology, mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score
OncoType DX® for DCIS	0045U	Oncology (breast ductal carcinoma in situ), mRNA, gene expression profiling by realtime RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score.
EndoPredict®	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

Test Name	CPT Codes	Breast Cancer Recurrent Predictive Genetic Test Description
Mammaprint™	81521	Oncology (breast), MRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis.
	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 (For dates of service on or after 01/01/2022)
Prosigna	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
BCI℠	81518	Oncology, mRNA, gene expression profiling by real-time RT-PCR of 11 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy

ICD-10 Diagnosis Codes

For the current ICD-10 listings for the above tests, please access the following LCA.
Diagnosis for **OncoTypeDX**® for CPT 81519, see LCA A55230.
Diagnosis for **OncoType DX® for DCIS**, for CPT 0045U, see LCA A57583.
Diagnosis for **EndoPredict®** for CPT 81522, see LCA A57567.
Diagnosis for **Mammaprint™** for CPT 81521, see LCA A55175.
Diagnosis for **Prosigna** for CPT 81520, see LCA A57560
Diagnosis for **Breast Cancer Index (BCI)** for CPT 81518, see LCA A56335.

Reviewed by / Approval Signatures

Population Health & Clinical Quality Committee: Clinton White, MD
Medical Director: Jim Romero, MD
Date Approved: 12-11-2024

References

1. WPS, MoIDX: Molecular Diagnostic Tests (MDT) (L36807), Revision History Date, 04/27/2023, R#15, [Cited 10/21/2024]
    a. Related Article: **Oncotype DX®** Breast Cancer Assay Billing and Coding Guidelines (A55230), Effective Date 02/16/2017, Revision date: 10/19/2021, Revision #R5. [Cited 10/21/2024]
    b. Related Article MoIDX: **MammaPrint** (A55175), Revision History Date: 01-21-2022, R#9. [Cited 10/21/2024]
2. WPS, MoIDX: OncoType DX® Breast Cancer for **DCIS** (Genomic Health™) (L37199), Revision Date:10/28/2021, Revision #R4. Related LCA (A57583) Updated on 10/28/2021, R1, original effective date 11/01/2019 [Cited 10/21/2024]
3. MoIDX: EndoPredict® Breast Cancer Gene Expression Test (L37663), Revision Date: 04/27/2023, R#7. Related Article A57567, Revision date 04/27/2023 R4 [Cited 10/21/2024]

4. MoIDX: Breast Cancer Assay: Prosigna (L36811), Revision Date: 03/30/2023, Revision #R5. Related Local Coverage Article: MoIDX: Breast Cancer Assay: Prosigna (A57560), Revision date: 03/30/2023, R2. [Cited 10/21/2024]
5. Local Coverage Determination (LCD, Biomarkers for Oncology (L35396), Effective Date: 10/01/2015, Revision Date:12/13/2020, Revision #R32. Related article (A52986), Version date: 10/01/2022, R38. [Cited 10/21/2024]
6. CMS Local Coverage Determination, MoIDX: Breast Cancer Index℠ Genetic Assay (L37913), Revision Date: 02/23/2023, R#3. Related Article MOIDX: Breast Cancer Index (BCI) Gene Expression Test (A56335). Revision Date: 10-30-2021, R#4. [Cited 10/21/2024]
7. Hayes, Oncotype DX Breast Recurrence Score (Genomic Health Inc.) for Lymph Node–**Positive** Patients, May 06, 2020, Annual review Apr 07, 2023. [Cited 10/21/2024]
8. Hayes, Oncotype DX Breast Recurrence Score for Lymph Node– **Negative** Patients (Genomic Health Inc.), Annual review: Apr 10, 2023. [Cited 10/21/2024]
9. Hayes, MammaPrint 70-Gene Breast Cancer Recurrence Assay (Agenda), Last review: March 16, 2018. Nov 28, 2018. [Cited 10/21/2024]
10. Hayes, EndoPredict (Myriad Genetics), Annual review: Oct 21, 2022. [Cited 10/21/2024]
11. Hayes, Prosigna Breast Cancer Prognostic Gene Signature Assay, Reviewed Sep 25, 2019, Jul 01, 2020. [Cited 10/21/2024]
12. Hayes, Oncotype DX Breast DCIS Score (Genomic Health Inc.), Annual Review Oct 21, 2022. [Cited 10/21/2024]
13. Hayes, Breast Cancer Index (BioTheranostics Inc.) for Lymph Node–Negative Patients, Annual review: May 11, 2022 [Cited 10/21/2024]
14. Hayes, Breast Cancer Index (BioTheranostics Inc.) for Lymph Node–Positive (1-3) Patients, Annual review: Jun 15, 2022. [Cited 10/21/2024]
15. NCCN, Clinical Practice Guidelines in Oncology, Breast Cancer, Version 4.2023 — March 23, 2023, [Cited 10/21/2024]

Publication History

07-31-19 New policy created to combine the Recurrent Predictive Genetic Testing for Breast Cancer. Note: No LCD criteria for Oncotype DX and Mammaprint in our Jurisdiction as of this date.

11-18-20 Annual review. Reviewed on 11-03-20. Title changed to include “Genetic Testing” at the beginning of title and “for Medicare” was removed. PHP will continue to follow the LCDs for all six tests. Coverage benefit changed to include Medicaid and Commercial members for: Oncotype-DX, ENDOPredict, and MammaPrint based on recommendation from Hayes or NCCN. Continue coverage for Medicare only for: OncotypeDX (DCIS), Prosigna. CPT code changed from 81599 to 81522 for EndoPredict. PA will be required for 81522. **Correction was made to Breast Cancer Index (BCI) on 02/16/2021, benefit was expanded to include Commercial and Medicaid. We will no longer follow LCD (L37913) since NCCN does not make a distinction of pre/post menopause.

11-17-21 Annual review. Reviewed by PHP Medical Policy Committee on 10/20/2021 and the following has been approved:
1. Oncotype DX: CPT 81519; continue to follow LCA A55230 for ALOB.
2. Oncotype DX (DCIS): CPT 0045U; coverage will continue for only Medicare. We will continue to follow LCD (L37199) and LCA (A57583); no utilization.
3. EndoPredict: CPT 81522, continue to follow LCD L37663 for ALOB; no utilization.
4. MammaPrint: CPT 81521; continue to follow LCA A55175 for ALOB.
5. Prosigna: Medicare will continue to follow LCD (L36811). Coverage extended for non-Medicare and will follow NCCN Breast Cancer guideline. CPT code 81520 (no utilization).
6. Breast Cancer Index (BCI): CPC 81518, continue to follow NCCN for ALOB. For benefit simplification we will follow NCCN for ALOB and not LCD L37913/LCA A56335.
Reviewed by Medical Policy Committee 12/01/2021: Specialty type configuration has been initiated and prior auth will no longer be required for: 81519, 0045U, 81522, 81521, 81520 and 81518.

11-16-22 Annual review. Reviewed by PHP Medical Policy Committee on 10/20/2021 and the following has been approved:
1. Oncotype DX: CPT 81519; continue to follow LCA A55230 for ALOB;
2. Oncotype DX (DCIS): coverage will continue for only Medicare. We will continue to follow LCD (L37199) and LCA (A57583); no utilization for 0045U.
3. EndoPredict: CPT 81522, continue to follow LCD (L37663) and LCA (A57567) for ALOB; no utilization.
4. MammaPrint: CPT 81521; continue to follow LCA A55175 for ALOB. No change to criteria. The LCA made update to the following: The second paragraph of the LCA was revised to

read, “MammaPrint® is a diagnostic test that analyzes the gene expression profile of FFPE breast cancer tissue samples to assess a patient's risk for distant metastasis” and a new third paragraph was added. LCA added code “For dates of service on or after 01/01/2022, use CPT code 81523 for the test if performed by NGS.” Code (81523) added to policy which already requires PA.

5. Prosigna: Change. Have non-Medicare to also follow LCD (L36811); LCA (A57560); LCD (L35396), and LCA (A52986) so all LOB will follow CMS. Non-Medicare will no longer follow NCCN Breast Cancer guideline. Continue PA for code 81520 (no utilization).
6. Breast Cancer Index (BCI): CPC 81518, continue to follow NCCN for ALOB. For benefit simplification we will continue to follow NCCN for ALOB and not LCD (L37913)/LCA (A56335).
   Specialty type configuration is pending to no longer require PA for: 81519, 0045U, 81522, 81521, 81520 and 81518 and configure ICD-10 to map to CPT using applicable LCA.

12-13-23 Annual review. Reviewed by PHP Medical Policy Committee on 10/18/2023.

- OncoType DX® - No change. Continue to follow Oncotype DX® Breast Cancer Assay LCA (A55230) for ALOB. No config update, continue CY 2022 config for code (81519) since no change to LCA A55230.
- OncoType DX® for DCIS- No change. Continue to follow Oncotype DX® Breast Cancer for DCIS assay LCD (L37199) and LCA (A57583) for Medicare only. No config update, continue CY 2022 config for code (0045U) for ALOB since no change to LCA (A57583).
- EndoPredict® - Change. Medicaid and commercial will not follow LCD but will follow NCCN. Medicare will continue to follow EndoPredict® Breast Cancer Gene Expression Test LCD (L37663), related article (A57567). Continue CY 2022 config for code (81522) for ALOB since LCA (A57567) made no change to ICD-10 on recent update from R3 to R4
- Mammaprint™ - No change- Continue to follow MammaPrint LCA (A55175) for ALOB. Continue CY 2022 config for code (81521 and 81523).
- Prosigna – Change. Medicaid and commercial will not follow LCD but will follow NCCN. Medicare will continue to follow Prosigna, (L36811) and (A57560). Continue CY 2022 config for code 81520.
- Breast Cancer Index (BCI)- Change. Medicare will now follow LCD (L37913 and LCA (A56335). Medicaid and commercial will continue to follow NCCN. Continue CY 2022 config for code 81518.
  No change to previous config set in CY 2022 to map ICD-10 to the CPT codes for all LOB using the following LCAs, so to remove PA requirement: 81519 = LCA (A55230); 0045U = LCA (A57583); 81522 = LCA (A57567); 81521 and 81523 = LCA (A55175); 81520 = LCA (A57560); and 81518 = LCA (A56335).

12-11-24 Annual review. Reviewed by PHP Medical Policy Committee on 10/23/2024. Continue following set criteria for all lines of business. Continue current configuration. MPC will manage configuration on this policy per the LCD/LCAs outlined in the policy.

This Medical Policy is intended to represent clinical guidelines describing medical appropriateness and is developed to assist Presbyterian Health Plan and Presbyterian Insurance Company, Inc. (Presbyterian) Health Services staff and Presbyterian medical directors in determination of coverage. The Medical Policy is not a treatment guide and should not be used as such.

For those instances where a member does not meet the criteria described in these guidelines, additional information supporting medical necessity is welcome and may be utilized by the medical director in reviewing the case. Please note that all Presbyterian Medical Policies are available online at: ***Click here for Medical Policies***

Web links:

At any time during your visit to this policy and find the source material web links has been updated, retired or superseded, PHP is not responsible for the continued viability of websites listed in this policy.

When PHP follows a particular guideline such as LCDs, NCDs, MCG, NCCN etc., for the purposes of determining coverage; it is expected providers maintain or have access to appropriate documentation when requested to support coverage. See the References section to view the source materials used to develop this resource document.