STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Gene Expression Profiling for the Management of Breast Cancer
LAB-002

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	7/11/2013
Revision Number:	12	**Last Rev Date:**	7/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	7/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	7/17/2020

Descriptive Narrative

Clinical features that guide decision to use chemotherapy

Most instances of estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-negative breast cancer <1 cm in size, and all cancers ≤0.5 cm in size, have a good prognosis with endocrine therapy alone, and do not typically require adjuvant chemotherapy. At the other end of the risk spectrum, most women with stage III breast cancers will warrant adjuvant chemotherapy because of their risk of recurrence and the likely benefits of chemotherapy treatment. Most cases of ER-positive breast cancer fall in between these two extremes, and decisions regarding the addition of chemotherapy to adjuvant endocrine therapy should be individualized based on patient and disease factors. Gene expression profiles performed in women with ER-positive, HER2-negative disease are useful when the decision regarding whether to use chemotherapy is unclear.

When to use a gene expression profile

Gene expression Oncotype DX Recurrence Score (RS) and EndoPredict have been developed to identify patients with such a low chance of recurrence that the absolute benefit of chemotherapy may not justify the risk of toxicities. For the RS, prospective, randomized clinical trials do not demonstrate that women with low scores (less than 26) benefit from the addition of chemotherapy. By contrast, patients with higher scores on these assays have a sufficiently high risk of recurrence despite endocrine therapy that the addition of chemotherapy outweighs the risk of toxicities.

These assays should not be used in women who are not candidates for chemotherapy since the results would not alter management. This might include patients with absolute contraindications to chemotherapy due to baseline health concerns or frailty, or women who for other reasons will not consider chemotherapy.

The Breast Cancer Index can be used to predict which patients are likely to benefit from extension of adjuvant anti-estrogen therapy beyond 5 years (NCCN Level of Evidence 2A).

Criteria

Gene expression profiling for the management of breast cancer is medically necessary when **ALL** the following are met:

1. The tumor is either ER-positive or progesterone receptor (PR)-positive, or both are positive; **AND**
2. The tumor is HER2 negative; **AND**
3. **ONE** of the following:
   a. Tumor is ≥0.6 cm to ≤1 cm in diameter with moderate/poor differentiation; **OR** b. Tumor ≥1 cm in diameter; **AND**
4. **ONE** of the following:
   a. Axillary lymph nodes are negative (pNO); **OR**
   b. Axillary lymph nodes contain ≤2 mm micrometastases (PN1 mi); **OR**
   c. Members with 1-3 axillary lymph nodes; **AND**
5. Member is a candidate for adjuvant chemotherapy or adjuvant endocrine therapy.

Gene expression profiling for the management of breast cancer is not medically necessary in any of the following situations:

1. Repeat testing for the same tumor.
2. Members with bilateral breast tumors.
3. The member is not a candidate for adjuvant chemotherapy.
4. When the initial surgery and biopsy were performed more than 6 months prior to ordering gene expression profiling.
5. When there are multiple ipsilateral tumors, multiple tests for each tumor type are not medically necessary. Only the tumor with the most aggressive histologic characteristics should be tested.
6. Testing should not be performed on a preliminary biopsy. Testing should be requested only when the tumor has been surgically removed and a pathology examination and report have been completed.

Coding

The following list of codes is provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

CPT	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.
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.

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual and as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

EncoderPro Optum 360.

NCCN Clinical Practice Guidelines in Oncology™ (NCCN). © 2021 National Comprehensive Cancer Network, Inc. Breast Cancer (V2.2022). Revised December 20, 2021.

Foukakis T, Bergh J, Hurvitz S. Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer. UpToDate, topic last updated: Apr 15, 2020.

Foukakis T, Bergh J, Hurvitz S. Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer. UpToDate, topic last updated: Apr 15, 2020.

Myriad EndoPredict® Technical Specifications Myriad Genetic Laboratories, Inc. Effective Date: December 10, 2019.

Harris LN, Ismaila N, McShane LM, et al. Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2016; 34:1134.

Kalinsky K. Barlow WE Gralow JR et. al. 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. New England Journal of Medicine. December 1, 2021. DOI: 10.1056/NEJMoa2108873v.

Hologic: Breast Cancer Index (company website). https://www.breastcancerindex.com/what-to-expect

MolDX: Breast Cancer Index Gene Expression Test. LCD L27824. Effective Date October 28, 2021.

LCD - MolDX: Breast Cancer Index® (BCI) Gene Expression Test (L37824) (cms.gov)

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
Signature			

Change Date	Changed By	Description of Change	Version
Signature			

Change Date	Changed By	Description of Change	Version
7/19/2024	CAC	Annual review. Added link to Hologic and LCD- MolDX In References section	12
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
7/21/2023	CAC	Annual review.	11
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
1/20/2023	Medical Director	Annual review. Added BCI to Descriptive Narrative and References sections. Added code 81518.	10
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/21/2022	Medical Director	Added Hologic Breast Cancer Index reference.	9
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
7/15/2022	CAC	Annual review.	8
Signature William (Bill) Jagiello, DO			

Criteria Change History (continued)

Change Date	Changed By	Description of Change	Version
7/16/2021	CAC	Annual review. Formatting changes.	7
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
7/17/2020	Medical Director	Title changed, added narrative, revised criteria, references updated.	6
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
7/15/2016	Medical Director	Criterion #5 added "or progesterone positive or both".	5
Signature C. David Smith, MD			

Change Date	Changed By	Description of Change	Version
7/17/2015	CAC	Added last paragraph in References.	4
Signature			

Change Date	Changed By	Description of Change	Version
7/14/2015	Medical Director	Added NCCN reference.	3
Signature			

Change Date	Changed By	Description of Change	Version
10/18/2013	CAC	Criteria renamed with generic name of 21-gene RT-PCR (real-time polymerase chain reaction) Assay (Oncotype DX®).	2
Signature			

Change Date	Changed By	Description of Change	Version
3/4/2013	Medical Director	Review by oncology consultant. Approved by CAC.	1
Signature			