EFFECTIVE DATE: 09|01|2026
POLICY LAST REVIEWED: 05|20|2026

OVERVIEW

Laboratory tests have been developed to detect the expression, via messenger RNA, of different genes in breast tumor tissue and combine the results-to determine prognosis in individuals with breast cancer. Test results may help providers and individuals decide whether to include adjuvant chemotherapy in the postsurgical management of breast cancer, to alter treatment in individuals with ductal carcinoma in situ (DCIS) or triple-negative (estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2) breast cancer (TNBC), or to recommend extended endocrine therapy in individuals who are recurrence-free at five years.

The following tests are addressed in this policy:

- DCISionRT® (Prelude Corporation) (CPT code 0295U)
- BluePrint® Molecular Subtyping Test (Agendia® Inc.) (CPT code 0630U)

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products

The following test(s) are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products as the evidence is insufficient to determine the effects of the technology on health outcomes:

- DCISionRT
- BluePrint® Molecular Subtyping Test

Commercial Products

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. **§27-19-81** described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for laboratory tests and applicable not covered/not medically necessary benefits/coverage.

BACKGROUND

Newly Diagnosed Breast Cancer

Per the Centers for Disease Control, breast cancer is a disease in which cells in the breast grow out of control, and can be found in the lobules, ducts, and connective tissue. Breast cancer affects individuals of all races and ethnicities and sexes. New cases are highest among White women (138.2 per 100,000) followed by Black

women (132 per 100,000). Rates of death from breast cancer, however, are highest among Black women (26.2 per 100,000) followed by Native Hawaiian or Other Pacific Islander women (25.1 per 100,000), and White women (18.8 per 100,000).

Breast cancer in men is rare, accounting for less than 1% of all breast cancer cases in the US. Still, 2,800 men will be diagnosed with breast cancer and 510 men will die from the disease in 2025. Black men have the highest breast cancer incidence (1.9 per 100,000) and mortality (0.5 per 100,000) of all racial and ethnic groups. Compared to women, men are more likely to be diagnosed with advanced (regional- or distant-stage) disease (48% vs. 31%), reflecting the absence of screening, as well as delays in diagnosis due to lack of awareness. The 5-year relative breast cancer survival rate is lower in men than women overall (84% vs. 91%, respectively) and for every stage of diagnosis.

Female Breast Cancer
The most common breast cancers are invasive ductal carcinoma and invasive lobular carcinoma. Less common types of breast cancer include Paget's disease, medullary, mucinous, and inflammatory. In ductal carcinoma in situ (DCIS), the cancer cells are only in the lining of the ducts and have not spread to other tissues; DCIS may lead to invasive breast cancer. Most breast cancer diagnoses are female breast cancer diagnosed at a localized stage (confined to the primary site), with less diagnoses being regional (spread beyond the primary site or to regional lymph nodes) or distant (spread to other organs or remote lymph nodes). The Nottingham score is a histological scoring system reflecting the grade of breast cancers. It is a total of scores based on microscopic determination of tubule formation, nuclear pleomorphism, and mitotic activity with each given a score of 1 to 3. Thus, the lowest Nottingham score is 3 and the highest is 9, with higher values thought to predict more aggressiveness. Nottingham score of 3-5 is assigned Grade I, 6-7 assigned Grade II, and 8-9 assigned Grade III.

Most women with newly diagnosed breast cancer in the U.S. present with the early-stage or locally advanced (ie, nonmetastatic) disease. However, almost a third of women who are disease-free after initial local and regional treatment develop distant recurrences during follow-up. Current breast cancer treatment regimens involve systemic adjuvant chemotherapy, hormonal therapy, biologic therapy, or a combination, depending on patients' baseline levels of recurrence risk, hormonal markers, and risk tolerance.

BluePrint (80-gene expression assay)
Molecular subtyping profile or BluePrint is proposed for the evaluation of an individual's prognosis when diagnosed with breast cancer. The multigene profile classifies breast cancer into basal type, luminal type and ERBB type (HER2/neu positive) molecular subclasses to stratify an individual's risk to purportedly assist with treatment decisions. Aetna Agendia BluePrint has an 80-gene profile that classifies breast cancer into molecular subtypes. The profile separates tumors into Basal-type, Luminal-type and ERBB2-type subgroups by measuring the functionality of downstream genes for each of these molecular pathways to inform the physician of the potential effect of adjuvant therapy.

Early-Stage Node-Negative Invasive Breast Cancer
For individuals who have early-stage node-negative invasive breast cancer considering adjuvant chemotherapy who receive gene expression profiling with BluePrint (80-gene expression assay) in conjunction with MammaPrint or alone, the evidence includes a few observational studies with no direct evidence that BluePrint improves the net health outcome. Clinical utility of BluePrint is unknown, because it is unclear how this test will add to treatment decision making using currently available, accepted methods (eg, clinical and pathologic parameters). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Early-Stage Invasive Breast Cancer Considering Neoadjuvant Chemotherapy
For individuals who have early-stage invasive breast cancer considering neoadjuvant systemic therapy who receive gene expression profiling with BluePrint (80-gene expression assay) in conjunction with MammaPrint or alone, the evidence includes an analysis from the I-SPY2 trial, with no direct evidence that BluePrint improves the net health outcome. In this trial, pCR were higher in BluePrint Basal-type versus Luminal-type

(34% vs 10%). At a median follow-up of 4.8 years, achieving pCR was associated with improved distant recurrence-free survival. However, the clinical utility of BluePrint is unknown, because it is unclear how this test will add to treatment decision making using currently available, accepted methods (eg, clinical and pathologic parameters). Additional Simon et al (2009) category A or B studies are required. Additionally, further clarity about how the test would inform clinical practice is still needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

DCISionRT

The DCISionRT combines 7 monoclonal protein markers (COX-2, FOXA1, HER2, Ki-67, p16/INK4A, PR, and SIAH2) assessed in tumor tissue with 4 clinicopathologic factors (age at diagnosis, tumor size, palpability, and surgical margin status) to produce a score that stratifies individuals with DCIS into 3 risk groups: low risk, elevated risk with good response, and elevated risk with poor response. The purpose of the test is to predict radiation benefit in individuals with DCIS following breast conserving surgery.

Ductal Carcinoma In Situ

For individuals who have DCIS considering radiotherapy who receive gene expression profiling with DCISionRT, the evidence includes retrospective validation studies. One Simon et al (2009) category B study provided evidence for clinical validity which showed no benefit of radiation therapy among a group of participants classified as low risk using the DCIS RT score at a threshold of <3 (absolute risk difference for invasive recurrence 1.2% (-5.7% to 8.2%). However, it is unclear whether the estimated 10-year recurrence risk for this group (12.4%; 95% CI 7.2% to 20.8% for invasive recurrence) is low enough to consider hanging management or is estimated with sufficient precision. Conclusions are also limited because there are no comparison recurrence estimates for women based on the standard of care (risk predictions based on clinical algorithms). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CODING

Medicare Advantage Plans and Commercial Products

The following CPT code(s) are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products:

This code can be used for DCISionRT:

0295U Oncology (breast ductal carcinoma in situ), protein expression profiling by immunohistochemistry of 7 proteins (COX2, FOXA1, HER2, Ki-67, p16, PR, SIAH2), with 4 clinicopathologic factors (size, age, margin status, palpability), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a recurrence risk score

This code can be used for BluePrint® Molecular Subtyping Test:

0630U Oncology (breast), mRNA, gene expression profiling by micro-array of 80 genes (80 content and 465 housekeeping), utilizing formalin-fixed paraffin-embedded tissue (FFPE), algorithm reported as index that is diagnostic of a molecular subtype (luminal, basal, Her2) (New Code Effective 4/1/2026; prior to 4/1/2026, this test would be filed with CPT code 81479)

RELATED POLICIES

Biomarker Testing Mandate
Unlisted Procedures

PUBLISHED

Provider Update, July 2026
Provider Update, July 2025
Provider Update, September 2024
Provider Update, February/November 2023
Provider Update, February 2022

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): MolDX: Molecular Diagnostic Tests (MDT) (L35160)
2. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): MolDX: Proteomics Testing (A59641)
3. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Billing and Coding: MolDX: BLUEPRINT® Test (A55115)
4. Park KU, Somerfield MR, Anne N, et al. Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer: ASCO Guideline Update. J Clin Oncol. May 10 2025; 43(14): 1720-1741. PMID 40209128
5. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology Breast Cancer Version 1.2026
6. Korde LA, Somerfield MR, Carey LA, et al. Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline. J Clin Oncol. May 01 2021; 39(13): 1485-1505. PMID 33507815
7. Centers for Disease Control and Prevention. 2024. Breast Cancer Statistics. https://www.cdc.gov/breast-cancer/statistics/?CDC_AAref_Val=https://www.cdc.gov/cancer/breast/statistics/index.htm. Accessed November 17, 2025.
8. American Cancer Society. Breast Cancer Facts & Figures (2024-2025). Link: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2024/breast-cancer-facts-and-figures-2024.pdf. Accessed November 18, 2025.
9. Colleoni M, Sun Z, Price KN, et al. Annual Hazard Rates of Recurrence for Breast Cancer During 24 Years of Follow-Up: Results From the International Breast Cancer Study Group Trials I to V. J Clin Oncol. Mar 20 2016; 34(9): 927-35. PMID 26786933
10. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 5.2025. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November 11, 2025.
11. Burstein HJ, Lacchetti C, Anderson H, et al. Adjuvant Endocrine Therapy for Women With Hormone Receptor-Positive Breast Cancer: ASCO Clinical Practice Guideline Focused Update. J Clin Oncol. Feb 10 2019; 37(5): 423-438. PMID 30452337
12. Liedtke C, Mazouni C, Hess KR, et al. Response to neoadjuvant therapy and long-term survival in patients with triple-negative breast cancer. J Clin Oncol. Mar 10 2008; 26(8): 1275-81. PMID 18250347
13. Wolff AC, Hammond ME, Hicks DG, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol. Nov 01 2013; 31(31): 3997-4013. PMID 24101045
14. Wolff AC, Somerfield MR, Dowsett M, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: ASCO-College of American Pathologists Guideline Update. J Clin Oncol. Aug 01 2023; 41(22): 3867-3872. PMID 37284804
15. Davies C, Godwin J, Gray R, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet. Aug 27 2011; 378(9793): 771-84. PMID 21802721
16. Tormey DC, Gray R, Falkson HC. Postchemotherapy adjuvant tamoxifen therapy beyond five years in patients with lymph node-positive breast cancer. Eastern Cooperative Oncology Group. J Natl Cancer Inst. Dec 18 1996; 88(24): 1828-33. PMID 8961972
17. Fisher B, Dignam J, Bryant J, et al. Five versus more than five years of tamoxifen for lymph node-negative breast cancer: updated findings from the National Surgical Adjuvant Breast and Bowel Project B-14 randomized trial. J Natl Cancer Inst. May 02 2001; 93(9): 684-90. PMID 11333290
18. Stewart HJ, Prescott RJ, Forrest AP. Scottish adjuvant tamoxifen trial: a randomized study updated to 15 years. J Natl Cancer Inst. Mar 21 2001; 93(6): 456-62. PMID 11259471
19. Davies C, Pan H, Godwin J, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet. Mar 09 2013; 381(9869): 805-16. PMID 23219286
20. Jakesz R, Greil R, Gnant M, et al. Extended adjuvant therapy with anastrozole among postmenopausal breast cancer patients: results from the randomized Austrian Breast and Colorectal Cancer Study Group Trial 6a. J Natl Cancer Inst. Dec 19 2007; 99(24): 1845-53. PMID 18073378

21. Goss PE, Ingle JN, Martino S, et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med. Nov 06 2003; 349(19): 1793-802. PMID 14551341
22. Goss PE, Ingle JN, Martino S, et al. Randomized trial of letrozole following tamoxifen as extended adjuvant therapy in receptor-positive breast cancer: updated findings from NCIC CTG MA.17. J Natl Cancer Inst. Sep 07 2005; 97(17): 1262-71. PMID 16145047
23. Mamounas EP, Jeong JH, Wickerham DL, et al. Benefit from exemestane as extended adjuvant therapy after 5 years of adjuvant tamoxifen: intention-to-treat analysis of the National Surgical Adjuvant Breast And Bowel Project B-33 trial. J Clin Oncol. Apr 20 2008; 26(12): 1965-71. PMID 18332472
24. Tjan-Heijnen VCG, van Hellemond IEG, Peer PGM, et al. Extended adjuvant aromatase inhibition after sequential endocrine therapy (DATA): a randomised, phase 3 trial. Lancet Oncol. Nov 2017; 18(11): 1502-1511. PMID 29031778
25. Blok EJ, Kroep JR, Meershoek-Klein Kranenbarg E, et al. Optimal Duration of Extended Adjuvant Endocrine Therapy for Early Breast Cancer; Results of the IDEAL Trial (BOOG 2006-05). J Natl Cancer Inst. Jan 01 2018; 110(1). PMID 28922787
26. Gnant M, Fitzal F, Rinnerthaler G, et al. Duration of Adjuvant Aromatase-Inhibitor Therapy in Postmenopausal Breast Cancer. N Engl J Med. Jul 29 2021; 385(5): 395-405. PMID 34320285
27. Khosrow-Khavar F, Filion KB, Al-Qurashi S, et al. Cardiotoxicity of aromatase inhibitors and tamoxifen in postmenopausal women with breast cancer: a systematic review and meta-analysis of randomized controlled trials. Ann Oncol. Mar 01 2017; 28(3): 487-496. PMID 27998966
28. Amir E, Seruga B, Niraula S, et al. Toxicity of adjuvant endocrine therapy in postmenopausal breast cancer patients: a systematic review and meta-analysis. J Natl Cancer Inst. Sep 07 2011; 103(17): 1299-309. PMID 21743022
29. Tseng OL, Spinelli JJ, Gotay CC, et al. Aromatase inhibitors are associated with a higher fracture risk than tamoxifen: a systematic review and meta-analysis. Ther Adv Musculoskelet Dis. Apr 2018; 10(4): 71-90. PMID 29619093
30. Tjan-Heijnen VCG, Lammers SWM, Geurts SME, et al. Extended adjuvant aromatase inhibition after sequential endocrine therapy in postmenopausal women with breast cancer: follow-up analysis of the randomised phase 3 DATA trial. EClinicalMedicine. Apr 2023; 58: 101901. PMID 36992863
31. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Link: https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed November 18, 2025.
32. Simon RM, Paik S, Hayes DF. Use of archived specimens in evaluation of prognostic and predictive biomarkers. J Natl Cancer Inst. Nov 04 2009; 101(21): 1446-52. PMID 19815849
33. Kelly CM, Krishnamurthy S, Bianchini G, et al. Utility of oncotype DX risk estimates in clinically intermediate risk hormone receptor-positive, HER2-normal, grade II, lymph node-negative breast cancers. Cancer. Nov 15 2010; 116(22): 5161-7. PMID 20665886
34. Peto R, Davies C, Godwin J, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. Lancet. Feb 04 2012; 379(9814): 432-44. PMID 22152853
35. Pauker SG, Kassirer JP. Therapeutic decision making: a cost-benefit analysis. N Engl J Med. Jul 31 1975; 293(5): 229-34. PMID 1143303
36. Pauker SG, Kassirer JP. The threshold approach to clinical decision making. N Engl J Med. May 15 1980; 302(20): 1109-17. PMID 7366635
37. Simes RJ, Coates AS. Patient preferences for adjuvant chemotherapy of early breast cancer: how much benefit is needed?. J Natl Cancer Inst Monogr. 2001; (30): 146-52. PMID 11773309
38. Duric VM, Stockler MR, Heritier S, et al. Patients' preferences for adjuvant chemotherapy in early breast cancer: what makes AC and CMF worthwhile now?. Ann Oncol. Nov 2005; 16(11): 1786-94. PMID 16126738
39. Thewes B, Meiser B, Duric VM, et al. What survival benefits do premenopausal patients with early breast cancer need to make endocrine therapy worthwhile?. Lancet Oncol. Aug 2005; 6(8): 581-8. PMID 16054569

40. Henderson IC. Breast cancer: fundamentals of evidence-based disease management. New York: Oxford University Press; 2015.
41. Hamelinck VC, Bastiaannet E, Pieterse AH, et al. A Prospective Comparison of Younger and Older Patients' Preferences for Adjuvant Chemotherapy and Hormonal Therapy in Early Breast Cancer. Clin Breast Cancer. Oct 2016; 16(5): 379-388. PMID 27212474
42. 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. Dec 30 2004; 351(27): 2817-26. PMID 15591335
43. Paik S, Tang G, Shak S, et al. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. J Clin Oncol. Aug 10 2006; 24(23): 3726-34. PMID 16720680
44. Tang G, Shak S, Paik S, et al. Comparison of the prognostic and predictive utilities of the 21-gene Recurrence Score assay and Adjuvant! for women with node-negative, ER-positive breast cancer: results from NSABP B-14 and NSABP B-20. Breast Cancer Res Treat. May 2011; 127(1): 133-42. PMID 21221771
45. Sparano JA, Gray RJ, Makower DF, et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. N Engl J Med. Nov 19 2015; 373(21): 2005-14. PMID 26412349
46. Sestak I, Buus R, Cuzick J, et al. Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor-Positive Breast Cancer: A Secondary Analysis of a Randomized Clinical Trial. JAMA Oncol. Apr 01 2018; 4(4): 545-553. PMID 29450494
47. Sparano JA, Gray RJ, Makower DF, et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. N Engl J Med. Jul 12 2018; 379(2): 111-121. PMID 29860917
48. Sparano JA, Crager MR, Tang G, et al. Development and Validation of a Tool Integrating the 21-Gene Recurrence Score and Clinical-Pathological Features to Individualize Prognosis and Prediction of Chemotherapy Benefit in Early Breast Cancer. J Clin Oncol. Feb 20 2021; 39(6): 557-564. PMID 33306425
49. Stemmer SM, Steiner M, Rizel S, et al. Ten-year clinical outcomes in N0 ER+ breast cancer patients with Recurrence Score-guided therapy. NPJ Breast Cancer. 2019; 5: 41. PMID 31728408
50. Filipits M, Rudas M, Jakesz R, et al. A new molecular predictor of distant recurrence in ER-positive, HER2-negative breast cancer adds independent information to conventional clinical risk factors. Clin Cancer Res. Sep 15 2011; 17(18): 6012-20. PMID 21807638
51. Sgroi DC, Sestak I, Cuzick J, et al. Prediction of late distant recurrence in patients with oestrogen-receptor-positive breast cancer: a prospective comparison of the breast-cancer index (BCI) assay, 21-gene recurrence score, and IHC4 in the TransATAC study population. Lancet Oncol. Oct 2013; 14(11): 1067-1076. PMID 24035531
52. Zhang Y, Schnabel CA, Schroeder BE, et al. Breast cancer index identifies early-stage estrogen receptor-positive breast cancer patients at risk for early- and late-distant recurrence. Clin Cancer Res. Aug 01 2013; 19(15): 4196-205. PMID 23757354
53. Cardoso F, van't Veer LJ, Bogaerts J, et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. N Engl J Med. Aug 25 2016; 375(8): 717-29. PMID 27557300
54. 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. Apr 2021; 22(4): 476-488. PMID 33721561
55. Brufsky AM, Hoskins KF, Conter HJ, et al. MammaPrint predicts chemotherapy benefit in HR+HER2- early breast cancer: FLEX Registry real-world data. JNCI Cancer Spectr. Sep 01 2025; 9(5). PMID 40796181
56. Krijgsman O, Roepman P, Zwart W, et al. A diagnostic gene profile for molecular subtyping of breast cancer associated with treatment response. Breast Cancer Res Treat. May 2012; 133(1): 37-47. PMID 21814749
57. Whitworth P, Stork-Sloots L, de Snoo FA, et al. Chemosensitivity predicted by BluePrint 80-gene functional subtype and MammaPrint in the Prospective Neoadjuvant Breast Registry Symphony Trial (NBRST). Ann Surg Oncol. Oct 2014; 21(10): 3261-7. PMID 25099655
58. Wuerstlein R, Kates R, Gluz O, et al. Strong impact of MammaPrint and BluePrint on treatment decisions in luminal early breast cancer: results of the WSG-PRIMe study. Breast Cancer Res Treat. Jun 2019; 175(2): 389-399. PMID 30796651
59. Dowsett M, Sestak I, Lopez-Knowles E, et al. Comparison of PAM50 risk of recurrence score with oncotype DX and IHC4 for predicting risk of distant recurrence after endocrine therapy. J Clin Oncol. Aug 01 2013; 31(22): 2783-90. PMID 23816962

60. Gnant M, Filipits M, Greil R, et al. Predicting distant recurrence in receptor-positive breast cancer patients with limited clinicopathological risk: using the PAM50 Risk of Recurrence score in 1478 postmenopausal patients of the ABCSG-8 trial treated with adjuvant endocrine therapy alone. Ann Oncol. Feb 2014; 25(2): 339-45. PMID 24347518
61. Albain KS, Barlow WE, Shak S, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomised trial. Lancet Oncol. Jan 2010; 11(1): 55-65. PMID 20005174
62. Dowsett M, Cuzick J, Wale C, et al. Prediction of risk of distant recurrence using the 21-gene recurrence score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: a TransATAC study. J Clin Oncol. Apr 10 2010; 28(11): 1829-34. PMID 20212256
63. Nitz U, Gluz O, Christgen M, et al. Reducing chemotherapy use in clinically high-risk, genomically low-risk pN0 and pN1 early breast cancer patients: five-year data from the prospective, randomised phase 3 West German Study Group (WSG) PlanB trial. Breast Cancer Res Treat. Oct 2017; 165(3): 573-583. PMID 28664507
64. Nitz U, Gluz O, Clemens M, et al. West German Study PlanB Trial: Adjuvant Four Cycles of Epirubicin and Cyclophosphamide Plus Docetaxel Versus Six Cycles of Docetaxel and Cyclophosphamide in HER2-Negative Early Breast Cancer. J Clin Oncol. Apr 01 2019; 37(10): 799-808. PMID 30785826
65. Gnant M, Sestak I, Filipits M, et al. Identifying clinically relevant prognostic subgroups of postmenopausal women with node-positive hormone receptor-positive early-stage breast cancer treated with endocrine therapy: a combined analysis of ABCSG-8 and ATAC using the PAM50 risk of recurrence score and intrinsic subtype. Ann Oncol. Aug 2015; 26(8): 1685-91. PMID 25935792
66. Filipits M, Dubsky P, Rudas M, et al. Prediction of Distant Recurrence Using EndoPredict Among Women with ER + , HER2 - Node-Positive and Node-Negative Breast Cancer Treated with Endocrine Therapy Only. Clin Cancer Res. Jul 01 2019; 25(13): 3865-3872. PMID 31064782
67. Kalinsky K, Barlow WE, Gralow JR, et al. 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. N Engl J Med. Dec 16 2021; 385(25): 2336-2347. PMID 34914339
68. Ettl J, Anders SI, Hapfelmeier A, et al. First prospective outcome data for the second-generation multigene test Endopredict in ER-positive/HER2-negative breast cancer. Arch Gynecol Obstet. Dec 2020; 302(6): 1461-1467. PMID 32902674
69. Solin LJ, Gray R, Baehner FL, et al. A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast. J Natl Cancer Inst. May 15 2013; 105(10): 701-10. PMID 23641039
70. Wärnberg F, Karlsson P, Holmberg E, et al. Prognostic Risk Assessment and Prediction of Radiotherapy Benefit for Women with Ductal Carcinoma In Situ (DCIS) of the Breast, in a Randomized Clinical Trial (SweDCIS). Cancers (Basel). Dec 03 2021; 13(23). PMID 34885211
71. Weinmann S, Leo MC, Francisco M, et al. Validation of a Ductal Carcinoma In Situ Biomarker Profile for Risk of Recurrence after Breast-Conserving Surgery with and without Radiotherapy. Clin Cancer Res. Aug 01 2020; 26(15): 4054-4063. PMID 32341032
72. Vicini FA, Mann GB, Shah C, et al. A Novel Biosignature Identifies Patients With DCIS With High Risk of Local Recurrence After Breast Conserving Surgery and Radiation Therapy. Int J Radiat Oncol Biol Phys. Jan 01 2023; 115(1): 93-102. PMID 36115740
73. Bremer T, Whitworth PW, Patel R, et al. A Biological Signature for Breast Ductal Carcinoma In Situ to Predict Radiotherapy Benefit and Assess Recurrence Risk. Clin Cancer Res. Dec 01 2018; 24(23): 5895-5901. PMID 30054280
74. Shah C, Bremer T, Cox C, et al. The Clinical Utility of DCISionRT ® on Radiation Therapy Decision Making in Patients with Ductal Carcinoma In Situ Following Breast-Conserving Surgery. Ann Surg Oncol. Oct 2021; 28(11): 5974-5984. PMID 33821346
75. Esserman L, Gallant E, Alvarado M. Less Is More: The Evolving Surgical Approach to Breast Cancer. Am Soc Clin Oncol Educ Book. 2016; 35: e5-e10. PMID 27249759
76. Dowsett M, Sestak I, Regan MM, et al. Integration of Clinical Variables for the Prediction of Late Distant Recurrence in Patients With Estrogen Receptor-Positive Breast Cancer Treated With 5 Years of Endocrine Therapy: CTS5. J Clin Oncol. Jul 01 2018; 36(19): 1941-1948. PMID 29676944

77. Noordhoek I, Blok EJ, Meershoek-Klein Kranenbarg E, et al. Overestimation of Late Distant Recurrences in High-Risk Patients With ER-Positive Breast Cancer: Validity and Accuracy of the CTS5 Risk Score in the TEAM and IDEAL Trials. J Clin Oncol. Oct 01 2020; 38(28): 3273-3281. PMID 32706636
78. Filipits M, Nielsen TO, Rudas M, et al. The PAM50 risk-of-recurrence score predicts risk for late distant recurrence after endocrine therapy in postmenopausal women with endocrine-responsive early breast cancer. Clin Cancer Res. Mar 01 2014; 20(5): 1298-305. PMID 24520097
79. Sestak I, Cuzick J, Dowsett M, et al. Prediction of late distant recurrence after 5 years of endocrine treatment: a combined analysis of patients from the Austrian breast and colorectal cancer study group 8 and arimidex, tamoxifen alone or in combination randomized trials using the PAM50 risk of recurrence score. J Clin Oncol. Mar 10 2015; 33(8): 916-22. PMID 25332252
80. Sestak I, Dowsett M, Zabaglo L, et al. Factors predicting late recurrence for estrogen receptor-positive breast cancer. J Natl Cancer Inst. Oct 02 2013; 105(19): 1504-11. PMID 24029245
81. Esserman LJ, Yau C, Thompson CK, et al. Use of Molecular Tools to Identify Patients With Indolent Breast Cancers With Ultralow Risk Over 2 Decades. JAMA Oncol. Nov 01 2017; 3(11): 1503-1510. PMID 28662222
82. Bartlett JMS, Xu K, Wong J, et al. Validation of the Prognostic Performance of Breast Cancer Index in Hormone Receptor-Positive Postmenopausal Breast Cancer Patients in the TEAM Trial. Clin Cancer Res. Apr 15 2024; 30(8): 1509-1517. PMID 38345755
83. Sgroi DC, Carney E, Zarrella E, et al. Prediction of late disease recurrence and extended adjuvant letrozole benefit by the HOXB13/IL17BR biomarker. J Natl Cancer Inst. Jul 17 2013; 105(14): 1036-42. PMID 23812955
84. Bartlett JMS, Sgroi DC, Treuner K, et al. Breast Cancer Index and prediction of benefit from extended endocrine therapy in breast cancer patients treated in the Adjuvant Tamoxifen-To Offer More? (aTTom) trial. Ann Oncol. Nov 01 2019; 30(11): 1776-1783. PMID 31504126
85. Noordhoek I, Treuner K, Putter H, et al. Breast Cancer Index Predicts Extended Endocrine Benefit to Individualize Selection of Patients with HR + Early-stage Breast Cancer for 10 Years of Endocrine Therapy. Clin Cancer Res. Jan 01 2021; 27(1): 311-319. PMID 33109739
86. Schroeder B, Zhang Y, Stål O, et al. Risk stratification with Breast Cancer Index for late distant recurrence in patients with clinically low-risk (T1N0) estrogen receptor-positive breast cancer. NPJ Breast Cancer. 2017; 3: 28. PMID 28795152
87. Bartlett JMS, Sgroi DC, Treuner K, et al. Breast Cancer Index Is a Predictive Biomarker of Treatment Benefit and Outcome from Extended Tamoxifen Therapy: Final Analysis of the Trans-aTTom Study. Clin Cancer Res. May 02 2022; 28(9): 1871-1880. PMID 35144966
88. Sgroi DC, Treuner K, Zhang Y, et al. Correlative studies of the Breast Cancer Index (HOXB13/IL17BR) and ER, PR, AR, AR/ER ratio and Ki67 for prediction of extended endocrine therapy benefit: a Trans-aTTom study. Breast Cancer Res. Dec 16 2022; 24(1): 90. PMID 36527133
89. Delahaye LJMJ, Drukker CA, Dreezen C, et al. A breast cancer gene signature for indolent disease. Breast Cancer Res Treat. Jul 2017; 164(2): 461-466. PMID 28451965
90. Lehmann BD, Jovanović B, Chen X, et al. Refinement of Triple-Negative Breast Cancer Molecular Subtypes: Implications for Neoadjuvant Chemotherapy Selection. PLoS One. 2016; 11(6): e0157368. PMID 27310713
91. Masuda H, Baggerly KA, Wang Y, et al. Differential response to neoadjuvant chemotherapy among 7 triple-negative breast cancer molecular subtypes. Clin Cancer Res. Oct 01 2013; 19(19): 5533-40. PMID 23948975
92. Gluz O, Kuemmel S, Nitz U, et al. Nab-paclitaxel weekly versus dose-dense solvent-based paclitaxel followed by dose-dense epirubicin plus cyclophosphamide in high-risk HR+/HER2- early breast cancer: results from the neoadjuvant part of the WSG-ADAPT-HR+/HER2- trial. Ann Oncol. Jun 2023; 34(6): 531-542. PMID 37062416
93. Iwata H, Masuda N, Yamamoto Y, et al. Validation of the 21-gene test as a predictor of clinical response to neoadjuvant hormonal therapy for ER+, HER2-negative breast cancer: the TransNEOS study. Breast Cancer Res Treat. Jan 2019; 173(1): 123-133. PMID 30242578
94. Huppert LA, Wolf D, Yau C, et al. Pathologic complete response (pCR) rates for patients with HR+/HER2- high-risk, early-stage breast cancer (EBC) by clinical and molecular features in the phase II I-SPY2 clinical trial. Ann Oncol. Feb 2025; 36(2): 172-184. PMID 39477071

95. Dubsky PC, Singer CF, Egle D, et al. The EndoPredict score predicts response to neoadjuvant chemotherapy and neoendocrine therapy in hormone receptor-positive, human epidermal growth factor receptor 2-negative breast cancer patients from the ABCSG-34 trial. Eur J Cancer. Jul 2020; 134: 99-106. PMID 32502940
96. Toole MJ, Kidwell KM, Van Poznak C. Oncotype dx results in multiple primary breast cancers. Breast Cancer (Auckl). Jan 09 2014; 8: 1-6. PMID 24453493
97. Espinosa E, Vara JA, Redondo A, et al. Breast cancer prognosis determined by gene expression profiling: a quantitative reverse transcriptase polymerase chain reaction study. J Clin Oncol. Oct 10 2005; 23(29): 7278-85. PMID 16129846
98. Sestak I, Zhang Y, Schroeder BE, et al. Cross-Stratification and Differential Risk by Breast Cancer Index and Recurrence Score in Women with Hormone Receptor-Positive Lymph Node-Negative Early-Stage Breast Cancer. Clin Cancer Res. Oct 15 2016; 22(20): 5043-5048. PMID 27252417
99. Kittaneh M, Badve S, Caldera H, et al. Case-Based Review and Clinical Guidance on the Use of Genomic Assays for Early-Stage Breast Cancer: Breast Cancer Therapy Expert Group (BCTEG). Clin Breast Cancer. Jun 2020; 20(3): 183-193. PMID 32014370
100. Davey MG, Davey CM, Bouz L, et al. Relevance of the 21-gene expression assay in male breast cancer: A systematic review and meta-analysis. Breast. Aug 2022; 64: 41-46. PMID 35512428
101. Andre F, Ismaila N, Allison KH, et al. Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update. J Clin Oncol. Jun 01 2022; 40(16): 1816-1837. PMID 35439025

CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS

This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member's subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.