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Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer Corporate Medical Policy

File Name: Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer
File Code: 2.04.VT36
Origination: 03/2019
Last Review: 02/2021
Next Review: 02/2022
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Description/Summary

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 patients with breast cancer. Test results may help providers and patients decide whether to include adjuvant chemotherapy in the postsurgical management of breast cancer, to alter treatment in patients with ductal carcinoma in situ or triple-negative (estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2) breast cancer (TNBC), or to recommend extended endocrine therapy in patients who are recurrence-free at 5 years.

Policy

Coding Information

Attachment I - CPT® Table & Instructions

When a service may be considered medically necessary

The use of the Oncotype DX 21-gene espression, Endopredict, Breast Cancer Index, Mammparint or Prosigna assays to determine recurrence risk for deciding whether to undergo adjuvant chemotherapy in women with primary, invasive breast cancer may be considered **medically necessary when** meeting all of the following characteristics:

- Unilateral or bilateral tumor;
- hormone receptor-positive (ie, estrogen receptor-positive or progesterone receptor- positive);
- human epidermal growth factor receptor 2-negative;
- tumor size >0.5 cm;
- node-negative (lymph nodes with micrometastases [≤2 mm in size] are considered node-negative for this policy statement) OR with 1-3 involved axillary lymph nodes;

- who will be treated with adjuvant endocrine therapy (eg, tamoxifen, aromatase inhibitors);
- when the test result aids the patient in deciding on chemotherapy (ie, when chemotherapy is a therapeutic option);
- when ordered within 6 months after diagnosis, because the value of the test for making decisions regarding delayed chemotherapy is unknown.

The use of the Breast Cancer Index gene expression test for the management of postmenopausal women diagnosed with early-stage (TNM stage T1-3, pN0, M0), node-negative, non-relapsed, ER and/or PR-positive, HER2-negative breast cancer, who are being or will be treated with primary adjuvant endocrine therapy may be considered medically necessary.

The Oncotype DX, EndoPredict, the Breast Cancer Index, MammaPrint, and Prosigna assays should only be ordered on a tissue specimen obtained during surgical removal of the tumor and after subsequent pathology examination of the tumor has been completed and determined to meet the above criteria (ie, the test should not be ordered on a preliminary core biopsy). The test should be ordered in the context of a physician-patient discussion regarding risk preferences when the test result will aid in making decisions regarding chemotherapy.

For patients who otherwise meet the above characteristics but who have multiple ipsilateral primary tumors, a specimen from the tumor with the most aggressive histologic characteristics should be submitted for testing. It is not necessary to test each tumor; treatment is based on the most aggressive lesion.

When a service is considered investigational

All other indications for the 21-gene RT-PCR assay (ie, Oncotype DX), EndoPredict, the Breast Cancer Index, MammaPrint, and Prosigna, including determination of recurrence risk in invasive breast cancer patients with positive lymph nodes, patients with bilateral disease, or to consider the length of treatment with tamoxifen with the exception of the Breast Cancer Index, are considered **investigational**.

Use of a subset of genes from the 21-gene RT-PCR assay for predicting recurrence risk in patients with noninvasive ductal carcinoma in situ (ie, Oncotype DX® Breast DCIS Score) to inform treatment planning after excisional surgery is considered **investigational**.

The use of BluePrint in conjunction with MammaPrint or alone is considered **investigational**. The use of Insight TNBCtype to aid in making decisions regarding chemotherapy in women with triple-negative breast cancer is considered **investigational.** Use of gene expression assays in men with breast cancer is considered **investigational**.

Reference Resources

1. Blue Cross and Blue Shield Association Medical Policy MPRM 2.04.36 - Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer. Last updated December 2020. Reviewed 2/2021.

2. Breast Cancer Index Predicts Extended Endocrine Benefit to Individualize Selection of Patients with HR+ Early-stage Breast Cancer for 10 Years of Endocrine Therapy. Iris Noordhoek, Kai Treuner, Hein Putter, Yi Zhang, Jenna Wong, Elma Meershoek-Klein Kranenbarg, Marjolijn Duijm-de Carpentier, Cornelis J.H. van de Velde, Catherine A. Schnabel and Gerrit-Jan Liefers. Clin Cancer Res January 1 2021 27 (1) 311-319.

Document Precedence

Blue Cross and Blue Shield of Vermont (BCBSVT) Medical Policies are developed to provide clinical guidance and are based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. The applicable group/individual contract and member certificate language, or employer's benefit plan if an ASO group, determines benefits that are in effect at the time of service. Since medical practices and knowledge are constantly evolving, BCBSVT reserves the right to review and revise its medical policies periodically. To the extent that there may be any conflict between medical policy and contract/employer benefit plan language, the member's contract/employer benefit plan language takes precedence.

Audit Information

BCBSVT reserves the right to conduct audits on any provider and/or facility to ensure compliance with the guidelines stated in the medical policy. If an audit identifies instances of non-compliance with this medical policy, BCBSVT reserves the right to recoup all non- compliant payments.

Administrative and Contractual Guidance

Benefit Determination Guidance

Prior approval may be required and benefits are subject to all terms, limitations and conditions of the subscriber contract.

Incomplete authorization requests may result in a delay of decision pending submission of missing information. To be considered compete, see policy guidelines above.

NEHP/ABNE members may have different benefits for services listed in this policy. To confirm benefits, please contact the customer service department at the member's health plan.

Federal Employee Program (FEP): Members may have different benefits that apply. For further information please contact FEP customer service or refer to the FEP Service Benefit Plan Brochure. It is important to verify the member's benefits prior to providing the service to determine if benefits are available or if there is a specific exclusion in the member's benefit.

Coverage varies according to the member's group or individual contract. Not all groups are required to follow the Vermont legislative mandates. Member Contract language takes precedence over medical policy when there is a conflict.

If the member receives benefits through an Administrative Services Only (ASO) group, benefits may vary or not apply. To verify benefit information, please refer to the member's employer benefit plan documents or contact the customer service department. Language in the employer benefit plan documents takes precedence over medical policy when there is a conflict.

Policy Implementation/Update information

03/2019	New medical policy. External input received. Codes 81519, 81520, 81599 & S3854 require Prior Authorization.
07/2019	External Input received. Code 81521 requires PA.
02/2020	Policy statements remain unchanged. Added codes 81518 & 0045U require prior approval.
02/2021	Policy statement amended to include evidence and clinical input on use in pts with 1-3 positive lymph nodes and Breast Cancer Index additional indications and add TNBC type as investigational. Updated Coding table added codes: Added codes 81479, 81522, 81599, 84999 to require prior approval. Added codes 81518, 0045U, 0153U as investigational. Added codes 88360, 88361, 88367, 88368, 88381 as not requiring prior approval if medical necessity criteria are met.

Eligible providers

Qualified healthcare professionals practicing within the scope of their license(s).

Approved by BCBSVT Medical Directors Date Approved

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Attachment I
CPT® Coding Table & Instructions

The following codes will be considered medically necessary or investigational when applicable criteria have been met.			
CPT®	81479	Unlisted molecular pathology procedure	Requires Prior Approval
CPT®	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	Investigational
CPT®	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	Requires Prior Approval
CPT®	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	Requires Prior Approval
CPT®	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	Requires Prior Approval
CPT®	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	Requires Prior Approval
CPT®	81599	Unlisted multianalyte assay with algorithmic analysis	Requires Prior Approval
CPT®	84999	Unlisted chemistry procedure	Requires Prior Approval

CPT®	88360	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; manual	No Prior Approval Required
CPT®	88361	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; using computer-assisted technology	No Prior Approval Required
CPT®	88367	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), using computer-assisted technology, per specimen; initial single probe stain procedure	No Prior Approval Required
CPT®	88368	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; initial single probe stain procedure	No Prior Approval Required
CPT®	88381	Microdissection (ie sample preparation of microscopically identified target); manual	No Prior Approval Required
CPT®	0045U	Oncology (breast ductal carcinoma in situ), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score	Investigational
CPT®	0153U	Oncology (breast), mRNA, gene expression profiling by next-generation sequencing of 101 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a triple negative breast cancer clinical subtype(s) with information on immune cell involvement	Investigational

HCPCS	S3854	Gene expression profiling panel for use in the management of breast cancer treatment	Requires Prior Approval