Geisinger

Geisinger Health Plan Policies and Procedure Manual

Policy: MP170

Section: Medical Benefit Policy

Subject: Gene Expression Profiling for Breast Cancer Treatment

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I. Policy: Gene Expression Profiling for Breast Cancer Treatment

II. Purpose/Objective:

To provide a policy of coverage regarding Gene Expression Profiling for Breast Cancer Treatment

III. Responsibility:

A. Medical Directors
B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

(i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
(ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.
(iii) The service or benefit will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for members of the same age.

DESCRIPTION:
Conventionally, the prognosis of breast cancer patients is determined by age, tumor size, histology, status of axillary lymph nodes, histologic type and hormone receptor status. More recently, investigation has focused on examining the gene expression in tumor tissue as a prognostic factor to predict a patient's chance of recurrence. Examples of this type of testing include Oncotype Dx®, Prosigna® Breast Cancer Assay, EndoPredict®, MammaPrint®, and a 76-gene signature.

CRITERIA FOR COVERAGE:

Oncotype DX™ Breast Assay; EndoPredict:
The Plan considers Oncotype DX™ Breast Cancer Assay gene expression profiling for breast cancer treatment as medically necessary to assess the need for adjuvant chemotherapy in newly diagnosed breast cancer when **ALL** of the following are met:

- A clinical diagnosis of Stage I , Stage II or Stage IIIa is made; **and**
- The tumor is estrogen receptor (ER) and/or progesterone receptor (PR) positive; **and**
- HER2 receptor status is negative; **and**
- Tumor size is 0.5 to 1.0 cm with moderate/poor differentiation or unfavorable features; or tumor size > 1 cm **and**
- The member is node negative, or staged at pN1mi (micrometastasis of 0.2-2.0mm)*, or with no more than three positive nodes ; **and**
- The member is a candidate for possible adjuvant chemotherapy (i.e. chemotherapy is not precluded due to other factors), and testing is being done specifically to guide the decision as to whether or not adjuvant chemotherapy will be used; **and**
- Less than six months have elapsed since the initial diagnosis

* Members with micrometastases (isolated tumor cells in the lymph node) are considered to be node negative

Prosigna® Breast Cancer Assay:
The Plan considers Prosigna® Breast Cancer Assay gene expression profiling for breast cancer treatment as medically necessary to assess the need for adjuvant chemotherapy in newly diagnosed breast cancer when **ALL** of the following are met:

- Diagnosed with Stage I or II breast cancer within the previous 6 months; **and**
- Node negative* or Stage II with 1-3 positive nodes; **and**
- Estrogen receptor (ER) positive or progesterone-receptor (PR) positive tumor; **and**
- Her2 negative tumor; **and**
- Tumor size 0.6 to 1.0 cm with moderate/poor differentiation or unfavorable features; or tumor size > 1 cm
- The member would be a candidate for adjuvant chemotherapy (i.e., chemotherapy is not contraindicated due to other factors); **and**
- The result of the test will guide the decision whether or not to use chemotherapy; **and**
- The member would choose to receive chemotherapy if offered.

* Members with micrometastases (isolated tumor cells in the lymph node) are considered to be node negative

MammaPrint® 70-Gene Breast Cancer Recurrence Assay
The Plan considers MammaPrint® Breast Cancer Assay gene expression profiling for breast cancer treatment as medically necessary to assess the need for adjuvant chemotherapy in newly diagnosed breast cancer when **ALL** of the following are met:

- A clinical diagnosis of Stage I or Stage II is made; **and**
- fresh or fresh frozen tissue is available; **and**
- tumor is estrogen receptor positive or progesterone receptor positive; **and**
- tumor is HER2 (human epidermal growth factor receptor 2) negative; **and**
- tumor size ≤ 5.0 centimeters; **and**
- the member is node negative or with 1-3 positive ipsilateral axillary lymph nodes; **and**
- the member would be a candidate for adjuvant chemotherapy (i.e., chemotherapy is not contraindicated due to other factors); **and**
- the result of the test will guide the decision whether or not to use chemotherapy; **and**
- the member would choose to receive chemotherapy if offered.

Breast Cancer Index™ (BCI)
The Plan considers Breast Cancer Index (BCI) as medically necessary for prediction of benefit from extended endocrine therapy when considering adjuvant systemic therapy for postmenopausal women with invasive breast cancer when **ALL** of the following criteria are met:

- Pathology reveals invasive carcinoma of the breast that is ER+ and/or PR+ and HER2-; and
- Member has early-stage disease (T1-3, pN0, M0); and
- member is lymph node negative; and
- member has no evidence of distant breast cancer metastasis (i.e., non-relapsed); and
- Test results will be used in determining treatment management of the member for chemotherapy and/or extension of endocrine therapy.

LIMITATIONS:
The test(s) are covered once per primary tumor, per individual.

FOR MEDICARE SEGMENTS: – CMS directives allow MammaPrint® 70 gene assay to be considered for coverage when used to predict recurrence risk in members with ER-positive or ER-negative, lymph node-negative breast cancer. Palmetto GBA established a formal coverage policy for all Medicare patients. This local carrier determination is applicable nationally.

Palmetto GBA, the designated national contractor for its Oncotype DX® breast cancer test, has expanded its coverage policy for all qualified Medicare patients to include patients with ductal carcinoma in situ (DCIS).

CMS directives allow Breast Cancer Index (BCI) Gene Expression Test to be considered for coverage when used to predict 10yr distant recurrence risk in members breast cancer. Palmetto GBA established a formal coverage policy for all Medicare patients. This local carrier determination is applicable nationally.

EXCLUSIONS:
Unless coverage is mandated, the Plan does NOT provide coverage for any other assays of genetic expression in breast tumor tissue (e.g. BluePrint ™, TargetPrint®, Mammostrat® Breast Cancer Test, BreastOncPx™, NexCourse® Breast IHC4, PreciseDx™ Breast Cancer Test, BreastPRS™, and the Rotterdam Signature 76-Panel) because they are considered experimental, investigational or unproven.

FOR MEDICAID BUSINESS SEGMENT:

- EndoPredict 12-gene molecular score is considered to be Experimental/Investigational and therefore **NOT COVERED**.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

Medicaid Business Segment:
Any requests for services, that do not meet criteria set in the PARP, will be evaluated on a case by case basis.

CODING ASSOCIATED WITH: *Gene Expression Profiling for Breast Cancer Treatment*
The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov ***or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.***

81479 Unlisted molecular pathology procedure (may be used to represent Mammostrat, Breast Cancer Index (BCI), BluePrint, TargetPrint)
84999 Unlisted Chemistry Procedure (may be used to represent Mammostrat, Breast Cancer Index (BCI), BluePrint, TargetPrint)
81599 Unlisted multianalyte assay with algorithmic analysis (may be used to represent Mammostrat, Breast Cancer Index (BCI), BluePrint, TargetPrint)
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 {*Breast Cancer Index (BCI*)}

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 {e.g., Oncotype DX(Genomic Health)}

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 {*e.g., Prosigna} (Prosigna Breast Cancer Prognostic Gene Signature Assay*)

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 {*Mammaprint*}

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 { *EndoPredict®}*

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 {*MammaPrint® NGS*}

S3854 Gene profiling for the use in the management of breast cancer treatment

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 {*EndoPredict, OncoTypeDX Breast DCIS Score Test* }

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 {*Insight TNBCtype*}

LINE OF BUSINESS:

Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

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This policy will be revised as necessary and reviewed no less than annually.

Devised: 01/12/06

Revised: 02/07, 7/07, 6/09(wording); 3/11 (criteria revision); 3/12 add Medicare mandate, revise criteria; 6/12 revise criteria; 11/14 (add DCIS coverage for Medicare); 9/15 (added Prosigna), 7/16 (Gender Language), 11/16 (Exclusions); 11/17 (add EndoPredict); 9/18 (expand MammaPrint indication, add Medicaid exclusion); 9/19 (update criteria, remove P/A); 9/20 (add Medicare coverage; exclusions); 3/21 (add BCI coverage)

Reviewed: 7/08, 8/13, 8/14, 3/22, 3/23, 3/24