APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member’s particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member’s benefit plan may contain specific exclusions related to the topic addressed in this CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any. All links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change prior to the annual review date. Lines of business (LOB) are subject to change without notice; current LOBs can be found at www.wellcare.com. All guidelines can be found at this site as well but selecting the Provider tab, then “Tools” and “Clinical Guidelines”.

BACKGROUND

In 2010, over 207,000 new cases of breast cancer among women in the United States while 39,840 died from the disease. With early detection, the 5-year survival rate for women with breast cancer is 98.6%; if the cancer spreads to the lymph nodes the 5-year survival drops to 83.8% and decreases drastically to 23.4% when the cancer metastasizes (NCI, 2011b). Due to the high rate of early detection prior to metastasis (93%), the overall 5-year survival rate is 89.1%; the number is 12% lower among black women.¹
MammaPrint (Agendia, BV, Amsterdam, Holland; also referred to as the “Amsterdam signature”), in 2010 became the only FDA-approved test for stage 1 and 2 breast cancer patients of all ages and is a predictor of disease outcome, especially in early stage breast cancer. The test identifies patients with early metastasis risk which is likely within 5 years following surgery; MammaPrint provides practitioners with a clear rationale to assess the benefit of chemotherapy in addition to other clinical information and pathology tests. (“FDA Expands Approval for MammaPrint Test,” 2010). A benefit of MammaPrint is the ability to influence the usage, or non-usage, of chemotherapy.2

The test measures the activity of 70 genes, providing information about the likelihood that cancer will recur. It measures each of these genes in a sample of a woman’s breast-cancer tumor and then uses a specific formula to produce a score that determines if the patient is deemed low-risk or high-risk for metastasis. In clinical trials, 1 in 4 women found to be at high risk by MammaPrint had recurrence of their cancer within 5 years. However, there are questions regarding the accuracy of this test. The positive predictive values at 5 and 10 years were 23% and 29%, respectively, while the corresponding negative predictive values were 95% and 90%, respectively.2

MammaPrint was tested on 307 patients under the age of 61 years who underwent surgery for stage I or stage II breast cancer, and who have tumor size equal to or less than 5 cm, and lymph node-negative. The study found that MammaPrint more than doubled physicians’ ability to predict breast cancer recurrence. Furthermore, a major clinical study is now underway to determine the tests efficacy in helping patients avoid needless chemotherapy; the European study will recruit 6,000 patients with early-stage breast cancer.2

American Society of Clinical Oncology (ASCO). In 2017 ASCO published an update to the recommendations of the use of tumor markers in the treatment and management of breast cancer. The key recommendations of the guideline update are as follows:4

- The use of the MammaPrint assay can be considered to inform decisions on adjuvant systemic chemotherapy in women with estrogen receptor-positive or progesterone receptor-positive, HER2-negative, node-negative breast cancer who are at a high clinical risk of recurrence per MINDACT categorization (details provided in Data Supplement published with this guideline).
- MammaPrint can also be considered in women with estrogen receptor-positive or progesterone receptor-positive, HER2-negative breast cancer with 1-3 positive lymph nodes who are at a high clinical risk of recurrence. Women meeting either of these criteria whose MammaPrint score is low may be treated with hormone therapy alone, as it is unlikely that chemotherapy will provide substantial additional benefits.
- MammaPrint should not be used in women who have a low clinical risk for recurrence per MINDACT categorization.

POSITION STATEMENT

Applicable To:
✔ Medicaid
✔ Medicare

Exclusions

- Members with low clinical risk category.
-Clinicians are recommended not to use the MammaPrint assay to guide decisions on adjuvant systemic therapy in members with hormone receptor-positive, HER2-negative, node-positive breast cancer at low clinical risk due to a lack of definitive data in this population or members with HER2-positive or triple-negative breast cancer.

Coverage

Use of the Breast Cancer Recurrent Assay (MammaPrint™) is considered medically necessary when the following criteria are met:

1. Members who have hormone receptor-positive, HER2-negative, node-negative breast cancer, especially those with high clinical risk in order to inform decisions on withholding adjuvant chemotherapy; OR,
2. Members with hormone receptor-positive, HER2-negative, node-positive breast cancer, particularly those with one to three positive nodes and a high clinical risk.

**Coding**

**CPT® Code**
- 0008M Oncology (breast), mRNA analysis of 58 genes using hybrid capture, on formalin-fixed paraffin-embedded (FFPE) tissue, prognostic algorithm reported as a risk score
- 81479 Unlisted molecular pathology procedure
- 81599 Unlisted multianalyte assay with algorithmic analysis (Unlisted maaa)
- 84999 Unlisted Chemistry Procedure when billed for MammaPrint

**HCPCS Level II Code**
- S3854 Gene expression profiling panel for use in the management of breast cancer treatment
  - *S- Codes are NON COVERED FOR MEDICARE*

**ICD-10-PCS Codes** – No applicable codes

**ICD-10-CM Diagnosis Codes**
- C50.011 Malignant neoplasm of nipple and areola, right female breast
- C50.012 Malignant neoplasm of nipple and areola, left female breast
- C50.021 Malignant neoplasm of nipple and areola, right male breast
- C50.022 Malignant neoplasm of nipple and areola, left male breast
- C50.111 Malignant neoplasm central portion of right female breast
- C50.112 Malignant neoplasm central portion of left female breast
- C50.121 Malignant neoplasm central portion of right male breast
- C50.122 Malignant neoplasm central portion of left male breast
- C50.129 Malignant neoplasm central portion of unspecified male breast
- C50.211 Malignant neoplasm of upper inner quadrant of right female breast
- C50.212 Malignant neoplasm of upper inner quadrant of left female breast
- C50.221 Malignant neoplasm of upper inner quadrant of right male breast
- C50.222 Malignant neoplasm of upper inner quadrant of left male breast
- C50.311 Malignant neoplasm of upper inner quadrant of right female breast
- C50.312 Malignant neoplasm of upper inner quadrant of left female breast
- C50.321 Malignant neoplasm of lower inner quadrant of right male breast
- C50.322 Malignant neoplasm of lower inner quadrant of left male breast
- C50.411 Malignant neoplasm of upper outer quadrant of right female breast
- C50.412 Malignant neoplasm of upper outer quadrant of left female breast
- C50.421 Malignant neoplasm of upper outer quadrant of right male breast
- C50.422 Malignant neoplasm of upper outer quadrant of left male breast
- C50.511 Malignant neoplasm of lower outer quadrant of right female breast
- C50.512 Malignant neoplasm of lower outer quadrant of left female breast
- C50.521 Malignant neoplasm of lower outer quadrant of right male breast
- C50.522 Malignant neoplasm of lower outer quadrant of left male breast
- C50.611 Malignant neoplasm of axillary tail of right female breast
- C50.612 Malignant neoplasm of axillary tail of left female breast
- C50.621 Malignant neoplasm of axillary tail of right male breast
- C50.622 Malignant neoplasm of axillary tail of left male breast
- C50.811 Malignant neoplasm of overlapping site of right female breast
- C50.812 Malignant neoplasm of overlapping site of left female breast
- C50.821 Malignant neoplasm of overlapping site of right male breast
- C50.822 Malignant neoplasm of overlapping site of left male breast
- C50.911 Malignant neoplasm of unspecified site of right female breast
- C50.912 Malignant neoplasm of unspecified site of left female breast
- C50.921 Malignant neoplasm of unspecified site of right male breast
- C50.922 Malignant neoplasm of unspecified site of left male breast
- Z17.0 Estrogen receptor positive status [ER+]
- Z17.1 Estrogen receptor negative status [ER-]

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal / state laws.
REFERENCES


2. 510(k) substantial equivalence determination decision summary. United States Food and Drug Administration 

3. Local coverage article for MolDx: MammaPrint billing and coding guidelines update (AS2557). Centers for 


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
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<tbody>
<tr>
<td>9/7/2017</td>
<td>Approved by MPC. Guidelines updated based on new directive from American Society of Clinical Oncology and removed out dated information from background.</td>
</tr>
<tr>
<td>5/2/2013</td>
<td>Approved by MPC. Applies to Medicaid only; for Medicare, see Palmetto LCD.</td>
</tr>
<tr>
<td>10/4/2012</td>
<td>Approved by MPC. Changed to E/I; no longer covered due to change by CMS.</td>
</tr>
<tr>
<td>9/2/2012</td>
<td>Approved by MPC. Clarified language regarding coverage of the test for certain indications per CMS LCD (Palmetto BGA, L30376).</td>
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<tr>
<td>12/1/2011</td>
<td>Approved by MPC. New guideline. New template design approved by MPC.</td>
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Clinical Coverage Guideline