Local Coverage Determination (LCD):
MolDX: BREAST CANCER Index℠ Genetic ASSAY (L35631)

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**Contractor Information**

<table>
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<tr>
<th>Contractor Name</th>
<th>Contract Type</th>
<th>Contract Number</th>
<th>Jurisdiction</th>
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**LCD Information**

- **LCD ID**: L35631
- **Original ICD-9 LCD ID**: L35294
- **LCD Title**: MolDX: BREAST CANCER Index℠ Genetic ASSAY

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**Document Information**

- **Original Effective Date**: For services performed on or after 10/01/2015
- **Revision Effective Date**: For services performed on or after 01/25/2016
- **Revision Ending Date**: N/A
- **Retirement Date**: N/A
- **Notice Period Start Date**: 12/10/2015
- **Notice Period End Date**: 01/24/2016

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CMS National Coverage Policy
Title XVIII of the Social Security Act, §1862(a)(1)(A) allows coverage and payment for only those services that are considered to be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.
Title XVIII of the Social Security Act, §1862(a)(1)(D) items and services related to research and experimentation.
Title XVIII of the Social Security Act, §1833(e), prohibits Medicare payment for any claim which lack the necessary information to process the claim.
42 CFR 410.32(a) Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions
42 CFR 411.15(k)(1) Particular services excluded from coverage.
CMS On-Line Manual, Publication 100-08, Medicare Program Integrity Manual, Chapter 3, §3.4.1.3, diagnosis code requirements.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

This policy limits coverage of the Breast Cancer Index℠ (aka BCI) (bioTheranostics) to patients that meet the following criteria:

- Post-menopausal female with non-relapsed, ER+ breast cancer, and
- Is lymph node negative, and
- Is completing five (5) years of tamoxifen therapy, and
- Patient must be eligible for consideration of extended endocrine therapy based on published clinical trial data or practice guidelines, and
- Physician or patient is concerned about continuing anti-hormonal therapy because of documented meaningful toxicity or possible significant patient-specific side effects, and
- The test results will be discussed with the patient (including the limitations of the testing method, the risks and benefits of either continuing or stopping the therapy based on the test, and current cancer management guidelines).

Claims for BCI testing will be denied when testing does not meet all of the above criteria.

Background

The body of evidence for the adjuvant endocrine treatment of ER+ breast cancer is continuing to evolve. Most recently, with the results of the ATLAS and aTTom trials, tamoxifen for an additional 5 years of adjuvant therapy has been added to the standard of care regimens as a NCCN recommendation to reduce late recurrences (defined as cancer recurring after 5 years of therapy).

The BCI assay (which was initially developed before ATLAS and aTTom data was available), uses PCR to interrogate selected proliferation-related and endocrine signaling-related genes, and may identify a subset of postmenopausal women who are at increased risk of late relapses for ER+ breast cancer and who may derive a greater benefit from extended hormone therapy. Current guidelines recommend adjuvant hormone therapy for postmenopausal patients with ER+ disease consisting of tamoxifen for 10 years (5 years initially and then strong consideration for an additional 5 years based on ATLAS and aTTom trials), aromatase Inhibitor (AI) for 5 years (ATAC), tamoxifen for 5 years followed by AI for 5 years (MA.17), or AI for 2-3 years followed by tamoxifen to complete 5 years. Extended (> 5 years) hormone therapy in each scenario is based on large randomized trials. Although there can be significant side effects of these therapies in some women, generally, the side effect profile is manageable when compared to the significant benefit of these interventions. The optimal sequence and duration of AI therapy, the benefit of tamoxifen after prolonged AI therapy, and result of tamoxifen use beyond 10 years remain unknown.
Although the BCI assay may identify a group of patients at highest risk of recurrence after 5 years post surgery it cannot be used independently without consideration of other clinical factors (such as age, tumor size and number of lymph nodes involved). A significant concern exists as to whether the assay can identify any group at such a low risk that it is safe to depart from a strong expert recommendation and safely stop therapy. Data from the prospective-retrospective review of the ATAC trial (trans-ATAC) shows a late recurrence risk in all patients, independent of risk category (BCI-H, BCI-I or BCI-L). Although the BCI-L group is lower than the others, it is still roughly 3.5% (but with 95% CI could be as high at 6.1%) and the annual risk of relapse steadily climbs in the years after stopping adjuvant endocrine therapy at 5 years. Given the substantial number of patients at risk in the BCI-Low group (over 60%), the total number of women at risk that may benefit from extended hormone therapy at the end of 5 years of tamoxifen therapy is not negligible.

Analysis of the prospective-retrospective review of MA.17 data, extended adjuvant therapy may be helpful in all groups studied. Although the H/I-low group did not meet statistical significance, the recurrence rate was decreased from 13% to 9% with the use of extended letrozole therapy with a relative risk reduction of 30%. In the H/I-High group the relative risk reduction was similar at 59%, which did meet statistical significance.

The risk BCI-C model developed from the trans-ATAC data provides a continuous risk predicted by the test. The risk curve is flat in only the very lowest BCI values. Starting around BCI of 2 (in the middle of the BCI-Low category), there is a linear increase in recurrence risk. At the 95% confidence interval (CI), the risk in some individuals categorized in the BCI-low group could be as high as 20%. Due to the data complexity, there is a significant possibility that a physician might consider all BCI-L patients at negligible risk, and thus not consider extended hormone therapy and consequently lead women from the NCCN recommended interventions. Given the low toxicity and low cost of extended therapy, the false sense of security could deny many women from lifesaving therapy.

In women who have received an AI for 5 years, data is lacking on the utility of extended adjuvant hormonal therapy.

The data defined benefit of the BCI test appears to be when a woman is having significant side effects or has other concerns regarding adjuvant tamoxifen therapy and is opposed to taking more than 5 years of tamoxifen or starting on an AI (letrozole) after tamoxifen. If the toxicity or concern of extending hormone therapy is significant then it may be reasonable to use the BCI test to help make a risk/benefit decision with the patient on continued adjuvant endocrine therapy. In the majority of patients, the toxicity of extended hormone therapy is tolerable especially in those who already have been on adjuvant hormonal therapy for 5 years. Even with the small benefit in all patients the MA.17, ATLAS and aTTom trials all demonstrated benefit from longer endocrine therapy. These trials established that the generally low toxicity of hormone therapy allows its long-term usage.

**BCI Use for Newly Diagnosed Breast Cancer Patients:**

It is possible that the BCI assay could identify patients who would most benefit from chemotherapy in the upfront setting, but this benefit has not been adequately studied. In one observational study the BCI risk recurrence level correlated with complete response to chemotherapy, but this trial does not provide sufficient evidence to warrant consideration for decision making in the newly diagnosed breast cancer patient. Further data will need to be published before the benefit of BCI can be confirmed or refuted in this setting.

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**Coding Information**

**Bill Type Codes:**

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

N/A

**Revenue Codes:**

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to

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apply equally to all Revenue Codes.

N/A

CPT/HCPCS Codes

**Group 1 Paragraph:** N/A

**Group 1 Codes:**
81479  Unlisted molecular pathology

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### ICD-10 Codes that Support Medical Necessity

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<th>Description</th>
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<td>Malignant neoplasm of nipple and areola, right female breast</td>
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<td>C50.012</td>
<td>Malignant neoplasm of nipple and areola, left female breast</td>
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<td>C50.019</td>
<td>Malignant neoplasm of nipple and areola, unspecified female breast</td>
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<tr>
<td>C50.111</td>
<td>Malignant neoplasm of central portion of right female breast</td>
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<td>C50.112</td>
<td>Malignant neoplasm of central portion of left female breast</td>
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ICD-10 Codes that DO NOT Support Medical Necessity

**Group 1 Paragraph:** BCI testing is non-covered for any indication other than those listed above.

**Group 1 Codes:** N/A

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ICD-10 Additional Information

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Revision History Information

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<th>Revision History Explanation</th>
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<td>R2</td>
<td>Removed lymph node negative coverage criteria. The lymph node negative criteria will be added in a revised draft policy and taken to CAC in October 2015.</td>
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<td>10/01/2015</td>
<td>R1</td>
<td>Added bullet point to the opening criteria to provide additional clarification of the clinical utility requirements.</td>
<td>Other (Clarification)</td>
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Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) A54765 - Response to Comments: MolDX: Breast Cancer Index? Genetic Assay (L35631) LCD(s) DL35631 - (MCD Archive Site)

Related National Coverage Documents N/A

Public Version(s) Updated on 12/03/2015 with effective dates 01/25/2016 - N/A Updated on 06/23/2015 with effective dates 10/01/2015 - 01/24/2016 Some older versions have been archived. Please visit the MCD Archive Site to retrieve them. Back to Top

Keywords

N/A Read the LCD Disclaimer Back to Top