Local Coverage Determination (LCD):
MolDX: Breast Cancer Index℠ Genetic Assay (L35631)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Palmetto GBA	A and B and HHH MAC	11202 - MAC B	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11302 - MAC B	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11402 - MAC B	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11502 - MAC B	J - M	North Carolina

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LCD Information

Document Information

LCD ID
L35631

Original ICD-9 LCD ID
N/A

LCD Title
MolDX: Breast Cancer Index℠ Genetic Assay

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

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
42CFR411.15(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 affect 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 letrazole 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 (letrazole) 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

apply equally to all Revenue Codes.

N/A
CPT/HCPCS Codes
Group 1 Paragraph: N/A

Group 1 Codes:
81479 Unlisted molecular pathology

ICD-10 Codes that Support Medical Necessity
Group 1 Paragraph: N/A

Group 1 Codes:

ICD-10 Codes	Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female 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
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female 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
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female 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
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
Z17.0	Estrogen receptor positive status [ER+]

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

ICD-10 Additional Information

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General Information

Associated Information
N/A

Sources of Information and Basis for Decision
References

1. Burstein HJ, Prestrud AA, Seidenfeld J, et al. American Society of Clinical Oncology clinical practice guideline: update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer. J Clin Oncol 2010; 28 (23):3784-96.

2. Davies C, 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. The Lancet, March 2013; 381(9869): 805-16. doi:10.1016/S0140-6736(12)61963-1.

3. Jankowitz RC, et al. Optimal systemic therapy for premenopausal women with hormone receptor-positive breast cancer. The Breast 2013;22:S165-70.

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5. Jerevall PL, et al. BCI Development and validation: Stockholm prospective study. Br J Cancer 2011;104:1762-1769.

6. Jin H, Tu D, Zhao N, et al. Longer-term outcomes of letrozole versus placebo after 5 years of tamoxifen in the NCIC CTG MA.17 trial: Analyses adjusting for treatment crossover. J Clin Oncol 2011; 30 (7):718-21.

7. Mathieu MC, et al. Breast Cancer Index predicts pathological complete response and eligibility for breast conserving surgery in breast cancer patients treated with neoadjuvant chemotherapy. Ann Oncol 2011. doi: 10.1093/annonc/mdr550

8. Strasser-Weippl K, et al. Extended adjuvant endocrine therapy in hormone-receptor positive breast cancer. The Breast 2013;22:S171-75.

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Revision History Information

Please note: Most Revision History entries effective on or before 01/24/2013 display with a Revision History Number of "R1" at the bottom of this table. However, there may be LCDs where these entries will display as a separate and distinct row.

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
01/25/2016	R3	Add lymph node negative to the coverage criteria	• Other (Returned to Oct CAC - Add lymph node negative to the coverage criteria)
10/01/2015	R2	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.	• Other (Legal Challenge)
10/01/2015	R1	Added bullet point to the opening criteria to provide additional clarification of the clinical utility requirements.	• Other (Clarification)

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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 - MolDX: Breast Cancer Index℠ Genetic Assay

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 Updated on 05/13/2015 with effective dates 10/01/2015 - 01/15/2016 Updated on 04/20/2015 with effective dates 10/01/2015 - N/A Back to Top

Keywords

N/A Read the **LCD Disclaimer** Back to Top