Local Coverage Determination (LCD):
MolDX: Breast Cancer Assay: Prosigna (L36380)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Noridian Healthcare Solutions, LLC	A and B MAC	01111 - MAC A	J - E	California - Entire State
Noridian Healthcare Solutions, LLC	A and B MAC	01112 - MAC B	J - E	California - Northern
Noridian Healthcare Solutions, LLC	A and B MAC	01182 - MAC B	J - E	California - Southern
Noridian Healthcare Solutions, LLC	A and B MAC	01211 - MAC A	J - E	American Samoa Guam Hawaii Northern Mariana Islands
Noridian Healthcare Solutions, LLC	A and B MAC	01212 - MAC B	J - E	American Samoa Guam Hawaii Northern Mariana Islands
Noridian Healthcare Solutions, LLC	A and B MAC	01311 - MAC A	J - E	Nevada
Noridian Healthcare Solutions, LLC	A and B MAC	01312 - MAC B	J - E	Nevada
Noridian Healthcare Solutions, LLC	A and B MAC	01911 - MAC A	J - E	American Samoa California - Entire State Guam Hawaii Nevada Northern Mariana Islands

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LCD Information

Document Information

Original Effective Date
For services performed on or after 05/03/2016

Revision Effective Date
For services performed on or after 01/01/2018

LCD ID

LCD Title
MolDX: Breast Cancer Assay: Prosigna

Revision Ending Date
N/A

Retirement Date
N/A

Proposed LCD in Comment Period
N/A

Notice Period Start Date
03/17/2016

Source Proposed LCD
N/A

Notice Period End Date
05/02/2016

CMS National Coverage Policy Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A), states that no Medicare payment shall be made for items or services that "are not 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, §1833(e), prohibits Medicare payment for any claim lacking the necessary documentation to process the claim.

42 Code of Federal Regulations (CFR) §410.32 Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

CMS Internet Online Manual Pub. 100-02 (Medicare Benefit Policy Manual), Chapter 15, Section 80, "Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests"

CMS Internet-Only Manuals, Publication 100-04, Medicare Claims Processing Manual, Chapter 16, §50.5 Jurisdiction of Laboratory Claims, 60.12 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance.

CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes".

Coverage Guidance
Coverage Indications, Limitations, and/or Medical Necessity

This policy provides limited coverage of the Prosigna breast cancer gene signature assay to patients that meet the following criteria consistent with the FDA indications for use:

- Post-menopausal female **either**

- ER+, lymph node-negative, stage I or II breast cancer; or
- ER+, lymph node-positive (1-3 positive nodes), stage II breast cancer.

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

Background

Women with early breast cancer and up to 3 locally positive lymph nodes whose tumor is estrogen-receptor positive will usually receive anti-hormonal therapy such as tamoxifen or aromatase inhibitors. U.S. (NCCN) and international (St. Gallen) guidelines predicate the decision for adjuvant chemotherapy on the size and grade of the breast cancer and other factors including genomic assays that provide additional information on risk of recurrence (Hernandez-Ava et al., 2013). According to a 2014 review, "Prognostic factors provide an indication of whether a patient needs subsequent therapy." (Paoletti & Hayes, 2014). Similarly, another 2014 review article states, "Efforts should be focused on reducing chemotherapy in patients unlikely to benefit." (Rampurwala et al., 2014). Accordingly, Medicare has covered breast cancer gene signature prognostic/predictive tests since 2006.

The PAM50 breast cancer gene signature test was developed in the late 1990s and initial studies showed a strong correlation with breast cancer recurrence and with complete pathologic response to neoadjuvant chemotherapy (Parker et al., 2009). While test results are reported on a scale of 1-100 as a Risk of Recurrence (ROR) score, the underlying algorithm is also able to classify cases into the luminal A and B, Her2neu, and triple-negative subtype classifications.

The Nanostring nCounter® nucleic acid analysis system replicates the PAM50 algorithm, as an FDA cleared kit, the Prosigna Breast Cancer Gene Signature Assay (FDA, 2013). The Prosigna package insert was most recently updated in January, 2015 (FDA, 2015) reflecting additional studies (Sestak et al., 2014). Notably, the Prosigna platform and the original PAM50 platform have a 0.997 correlation (Dowsett et al., 2013).

For the FDA, the Prosigna test was validated in a large population of post-menopausal, estrogen-receptor positive women based on 1,017 cases of the TransATAC study (Dowsett et al., 2013). The study showed a strong correlation with long-term breast cancer recurrence and added substantial additional prognostic information over a clinical treatment score based on standard clinical variables. This study was replicated in an independent population, also on the Prosigna test, using 1,620 samples from the ABCSG8 trial (Gnant, 2014). A separate analysis of these trials validated prediction of distant recurrence in years 5-10 after initial diagnosis (Sestak et al., 2014) and has been incorporated in the FDA labeling (FDA, 2015). The Prosigna test is issued as separate reports, consistent with FDA review and labeling, for node-negative and node-positive (1-3 node) populations. Analytic performance, precision, reproducibility, and analysis of the clinical validations are provided in the FDA labeling (FDA, 2013; FDA, 2015).

Clinical utility of this breast cancer gene signature has also been assessed. The study of Martin et al. (2015) showed a 20% decision impact on decisions for or against adjuvant chemotherapy in an all-comers population of 200 new cases of incident breast cancer, when Prosigna test information became available after all other clinical information had been considered. The net rates of selecting adjuvant chemotherapy for low, intermediate, and high risk cases was similar to that observed in a meta-analysis of Oncotype DX decision data (Carlson & Roth, 2013). Additional support for the use of these test results in treatment decisions comes from Parker et al. (2009), in which there was a strong association with neoadjuvant chemotherapy response. Low-scoring cases have a very low change of complete pathological response to neoadjuvant chemotherapy, while high-scoring cases approach a 50% chance of complete pathological response. The same findings have been observed for other breast cancer gene signatures based on prognostic algorithms (Chang et al., 2008).

Summary of Evidence

NA

Analysis of Evidence
(Rationale for Determination)

NA

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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.

0x TBD

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:

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
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

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

ICD-10 Codes	Description
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
D05.00	Lobular carcinoma in situ of unspecified breast
D05.01	Lobular carcinoma in situ of right breast
D05.02	Lobular carcinoma in situ of left breast
D05.10	Intraductal carcinoma in situ of unspecified breast
D05.11	Intraductal carcinoma in situ of right breast
D05.80	Other specified type of carcinoma in situ of unspecified breast
D05.90	Unspecified type of carcinoma in situ of unspecified breast

ICD-10 Codes that DO NOT Support Medical Necessity N/A
ICD-10 Additional Information Back to Top

General Information

Associated Information

Documentation Requirements

The patient's medical record must contain documentation that fully supports the medical necessity for services included within this LCD. (See "Coverage Indications, Limitations, and/or Medical Necessity") This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available to the MAC upon request.

This final LCD, effective 05/03/2016, combines JEA DL36320 into the JEB LCD so that both JEA and JEB contract numbers will have the same final MCD LCD number.

No comments were received for comment period ending 12/07/2015.

Sources of Information
References

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3. Dowsett M et al. (2013) Comparison of PAM50 Risk of Recurrence Score With Oncotype DX and IHC4 for Predicting Risk of Distant Recurrence After Endocrine Therapy. J Clin Oncol 31:2783-90.

4. FDA (2013). 510(k) Summary: K130010. Prosigna Breast Cancer Prognostic Gene Signature Assay.

5. FDA (2015) Package Insert: Prosigna Breast Cancer Prognostic Gene Signature Assay. Version 04, 18 pages. At: http://prosigna.com/docs/Prosigna_Packet_Insert_US.pdf

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11. Rampurwala MM et al. (2014) Update on adjuvant chemotherapy for early breast cancer. Breast Cancer 8:125-134.

12. Sestak I et al. (2014) Prediction of late recurrence after 6 years of endocrine treatment: combined analysis of patients from the ABCCSG8…using the PAM50 Risk of Recurrence Score. J Clin Oncol doi: 10.1200/JCO.2014.55.6894.

Bibliography

NA

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Revision History Information

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
01/01/2018	R1	2018 Annual CPT/HCPCS updates: Added 81520 to CPT/HCPCS codes section. 12/4/17: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.	• Creation of Uniform LCDs With Other MAC Jurisdiction • Revisions Due To CPT/HCPCS Code Changes

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Associated Documents

Attachments N/A

Related Local Coverage Documents LCD(s) DL36320 - (MCD Archive Site) DL36380 - (MCD Archive Site)

Related National Coverage Documents N/A

Keywords

- MolDX
- Breast
- Cancer
- Assay
- Prosigna
- Lymph
- Node
- 0008M

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