MolDX: Breast Cancer Assay: Prosigna

Noridian Healthcare Solutions, LLC

The ICD-10 codes for male breast cancer were erroneously included in the current draft LCD and will be removed when the LCD finalizes since Prosigna is not currently approved for use in the male breast cancer patient.

Please Note: This is a Proposed LCD.
Proposed LCDs are works in progress and not necessarily a reflection of the current policies or practices. Proposed LCDs in an approval status display on the CMS MCD for public review.

Contractor Information

Contractor Name	Noridian Healthcare Solutions, LLC
Contract Number	01112
Contract Type	A and B MAC
Associated Contract Numbers	(A and B MAC - 01182 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01212 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01312 - J - E) Noridian Healthcare Solutions, LLC

Proposed LCD Information

Source LCD ID N/A

Proposed LCD ID	DL36380
Original ICD-9 LCD ID	N/A
Proposed LCD Version	4
Proposed LCD Title	MolDX: Breast Cancer Assay: Prosigna
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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"

Jurisdiction California - Northern

Super MAC Jurisdiction J - E

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).

Proposed Process Information

Documentation Requirements

Associated Information

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 upon request to Noridian or other Medicare entity.

References

Sources of Information and Basis for Decision

1. Carlson JJ & Roth JA (2013). The impact of Oncotype DX breast cancer assay in clinical practice: a systematic review and meta-analysis. Breast Cancer Res Treat 141:13-22.

2. Chang JC et al. (2008) Gene expression patterns in formalin-fixed, paraffin-embedded core biopsies predict docetaxel chemosensitivity in breast cancer patients. Breast Cancer Res Treat108:233-40.

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

6. Gnant M et al. (2014) Predicting distant recurrence in receptor-positive breast cancer patients with limited clinicopathological risk: using the PAM50 Risk of Recurrence score in 1478 postmenopausal patients of the ABCSG-8 trial treated with adjuvant endocrine therapy alone. Ann Oncol 25:339–45.

7. Hernandez-Aya LF, Gonzalez-Angulo AM. Adjuvant systemic therapies in breast cancer. Surg Clin North Am . 2013 Apr; 93(2):473–91.

8. Martin M et al. (2015) Prospective study of the impact of the Prosigna assay on adjuvant clinical decision-making in unselected patients with estrogen receptor positive, human epidermal growth factor receptor negative, node negative early-stage breast cancer. Curr Med Res Opin 23:1-9.

9. Paoletti C & Hayes DF (2014) Molecular testing in breast cancer. Ann Rev Med 65:95-110.

10. Parker JS et al. (2009) Supervised risk predictor of breast cancer based on intrinsic subtypes. J Clin Oncol 27:1160-1167.

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.

1.

	Meeting Date	Meeting Information	State
Open Meetings	10/01/2015	Embassy Suites - Las Vegas Flamingo Ballroom 4315 Swenson Street Las Vegas, NV 89119	American Samoa, California - Entire State, Guam, Hawaii, Nevada, Northern Mariana Islands, California - Northern, California - Southern

Part B MAC Contractor Advisory Committee (CAC) Meetings	**Meeting Date**	**Meeting Information**	**State**
	10/21/2015	DoubleTree by Hilton San Francisco Airport Tiburon/Sausalito Room 835 Airport Boulevard Burlingame, CA 94010	California - Entire State, California - Northern, California - Southern

	10/09/2015	The Pacific Club, Card Room 1451 Queen Emma St Honolulu, HI 96813	American Samoa, Guam, Hawaii, Northern Mariana Islands
	10/22/2015	Clark County Medical Association/NV State Medical Association 2590 E Russell Rd Las Vegas, NV 89120	Nevada

Comment Period Start Date	10/01/2015
Comment Period End Date	12/07/2015
Released to Final LCD Date	Not yet released.
Reason for Proposed LCD	Creation of Uniform LCDs... Creation of Uniform LCDs With Other MAC Jurisdiction
Proposed LCD Contact	Noridian Healthcare Solutions, LLC JE Part B Contractor Medical Director(s) Attention: Draft LCD Comments PO Box 6783 Fargo, North Dakota 58108-6783 policyb.drafts@noridian.com

Coding Information

Bill Type Codes

Revenue Codes

Group 1: Paragraph

Group 1: Codes

CPT/HCPCS Codes	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

Does the CPT 30% Coding Rule Apply?	No

ICD-10 Codes that Support Medical Necessity

Note: Performance is optimized by using code ranges.

Group 1: Paragraph

Group 1: Codes

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
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male 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
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of 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
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified 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
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male 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
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified 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
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified 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
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified 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
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified 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
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male 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
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male 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

Group 1: Paragraph

Group 1: Codes

Note: Performance is optimized by using code ranges.

Additional ICD-10 Information

Associated Documents

Attachments	There are no attachments for this LCD.
Related Local Coverage Documents	This LCD version has no Related Local Coverage Documents.
Related National Coverage Documents	This LCD version has no Related National Coverage Documents.
All Versions	**Version 4 - Updated on 08/13/2015 06:52:11, by Cheryl.Ryan@noridian.com, with effective dates N/A - N/A (Approved).** Version 3 - Updated on 08/12/2015 16:48:17, by Christine.Burnside@noridian.com, with effective dates N/A - N/A. Version 2 - Updated on 08/12/2015 16:37:19, by Christine.Burnside@noridian.com, with effective dates N/A - N/A. Version 1 - Updated on 08/12/2015 16:26:57, by Christine.Burnside@noridian.com, with effective dates N/A - N/A.