Local Coverage Determination (LCD):
MolDX: Prolaris™ Prostate Cancer Genomic Assay (L36350)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Noridian Healthcare Solutions, LLC	A and B MAC	02101 - MAC A	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02102 - MAC B	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02201 - MAC A	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02202 - MAC B	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02301 - MAC A	J - F	Oregon
Noridian Healthcare Solutions, LLC	A and B MAC	02302 - MAC B	J - F	Oregon
Noridian Healthcare Solutions, LLC	A and B MAC	02401 - MAC A	J - F	Washington
Noridian Healthcare Solutions, LLC	A and B MAC	02402 - MAC B	J - F	Washington
Noridian Healthcare Solutions, LLC	A and B MAC	03101 - MAC A	J - F	Arizona
Noridian Healthcare Solutions, LLC	A and B MAC	03102 - MAC B	J - F	Arizona
Noridian Healthcare Solutions, LLC	A and B MAC	03201 - MAC A	J - F	Montana
Noridian Healthcare Solutions, LLC	A and B MAC	03202 - MAC B	J - F	Montana
Noridian Healthcare Solutions, LLC	A and B MAC	03301 - MAC A	J - F	North Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03302 - MAC B	J - F	North Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03401 - MAC A	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03402 - MAC B	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03501 - MAC A	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03502 - MAC B	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03601 - MAC A	J - F	Wyoming
Noridian Healthcare Solutions, LLC	A and B MAC	03602 - MAC B	J - F	Wyoming

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LCD Information

Document Information

LCD ID
L36350

LCD Title
MolDX: Prolaris™ Prostate Cancer Genomic Assay

Proposed LCD in Comment Period
N/A

Source Proposed LCD
N/A

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

Original Effective Date
For services performed on or after 10/15/2015

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

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
08/30/2015

Notice Period End Date
10/14/2015

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

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

Noridian will provide limited coverage for the Prolaris™ prostate cancer assay (Myriad, Salt Lake City, UT) to help determine which patients with early stage, needle biopsy proven prostate cancer, can be conservatively managed rather than treated with definitive surgery or radiation therapy.

Summary of Evidence

In 2014, nearly 233,000 men in the US will be diagnosed with prostate cancer, which accounts for 14% of all new cancer diagnosis. More than 29,000 men will die from this disease representing 5% of all cancer deaths. Gratefully 98.9% of men are surviving at 5 years.

Many individuals do not need treatment for their prostate cancer in as much as their prognosis is excellent even without treatment. However, physicians and patients struggle to know who can safely be observed versus the subgroup that needs more aggressive treatment to achieve cure, and recognize that definitive treatment for localized prostate cancer can have lifelong morbidities.

Traditionally, clinicopathologic characteristics are utilized to determine risk and subsequent treatment. Several nomograms have been introduced to try to determine who is at risk of developing metastatic disease and who, if treated early, could avoid this outcome. A representative one taken from the NCCN (and AUA), divides early prostate cancer into several groups based initially on life expectancy, with a second stratification using clinical

exam, reassessment of life expectancy, biopsy (Gleason score), PSA and imaging.

These groups are detailed below:

	Risk Category			
	Very Low	**Low**	**Intermediate**	**High**
Clinicopathologic Findings	• T1c **AND** • Gleason score ≤ 6 **AND** • PSA ≤ 10 ng/mL **AND** • < 3 prostate cores with tumor **AND** • ≤ 50% tumor in any core **AND** • PSA density of < 0.15 ng/mL/g	• T1-T2a **AND** • Gleason score ≤ 6/Gleason grade group 1 **AND** • PSA ≤ 10 ng/mL	• T2b-T2c **OR** • Gleason score 3+4= 7/Gleason grade group 2 **OR** • **OR** • PSA 10-20 ng/mL	• T3a **OR** • Gleason Score 8/Gleason grade group 4 **OR** • Gleason score 9-10/Gleason grade group 5 **OR** • PSA > 20 ng/mL
Treatment Options				
≥ 20 y life expectancy	• Active Surveillance • RT or Brachy • RP (± LND)			
≥ 10 y life expectancy	• Active Surveillance	• Active Surveillance • RT or Brachy • RP (± LND	• RP (± LND) • RT or Brachy ± Adj Horm	• RT + Adj Horm • RT + Brachy • RP + LND ± RT, ADT
< 10 y life expectancy	• Observation	• Observation	• RT or Brachy ± Adj Horm • Observation	• N/A

Table 1: NCCN 2017 V2 - Localized Prostate Cancer Risk Stratification and Treatment (PSA – Prostate Specific Antigen; RT – Radiation Therapy; RP – Radical Prostatectomy; LND – lymph node dissection; Adj Horm – Adjuvant Androgen Deprivation)

Use of these stratification and treatment approaches has led to high cure rates for early stage prostate cancer. Yet it is widely accepted that many men are over-treated to achieve the cure rate. In the PIVOT trial men with early prostate cancer, initially randomized to radical prostectomy or observation, showed that over 12 years there was no difference in absolute mortality between the groups. However, this study was hampered by several problems including:

- Only 731 of 5023 eligible patients chose to participate in the study based on randomization criteria.
- In the group randomized to RP: only 85% of the men received definitively therapy (79% surgery; 6% other).
- In the observational group: 10% of the observation group received RP initially and additional 20% eventual received definitive treatment.

- Despite broad inclusion criteria, > 50% of patients had a PSA of <10 (median PSA of 7) and had biopsy proven T1c disease. Although there were a significant number of patients with Gleason score ≥7 (25%), 40% of men were classified initially as being low risk; and 30% were intermediate.

Although subgroups were small, it appears that high-risk groups (including those with PSA > 10) benefitted from RP. Furthermore, there was a trend for the intermediate risk patients to benefit from RP as well. The small number of patients willing to enter the study, and the high rate of crossover (both initially and subsequently) demonstrates the difficulty of doing observation trials in the United States.

Prolaris™ Prostate Cancer Assay

Test Description

Prolaris™ is an RNA based assay measuring the expression of 31 cell cycle progression (CCP) genes and 15 "housekeeping" genes that act as internal controls and normalization standards in each patient sample. The assay is performed on formalin fixed paraffin-embedded (FFPE) prostate cancer blocks. The assay results are reported as a numerical score along with accompanying interpretive information.

Test Performance

The clinical performance of this assay was assessed in several retrospective validation studies. These include two British cohorts of men diagnosed with prostate cancer on biopsy and then treated conservatively; and an additional cohort of men diagnosed by TURP and conservatively managed. Further validation was performed in various other cohorts including men who underwent radical prostatectomy, and men treated with definitive radiotherapy. The Prolaris™ cell cycle progression score (CCP) was found to be an independent and more robust prognostic factor for disease related death than traditional clinicopathologic factors although disease stage and Gleason score consistently portended a more negative prognostic picture.

Due to the difficulty in obtaining prospective data in early prostate cancer (outcomes take decades to develop, hard to accrue patients to a conservatively managed arm in the US), and given the unmet need, clinical utility can be extrapolated from this retrospective data. Doing so is not without shortcomings. It is unclear how the British cohorts were followed or who went on to receive definitive therapy inside the observation groups. The U.K. standard of care for treating these prostate cancer patients is different. In the U.S. conservatively managed patients is not the common occurrence. Furthermore, the long time period to determine outcomes and the lack of tissue specimens make review of a U.S. cohort unlikely if not impossible for many years.

In several of the published cohorts including the conservatively managed patients, multivariate analysis identified CCP score and Gleason score as the only values that consistently identify increased risk of death from prostate cancer. It also should be noted that the cancer related death rate in these retrospective studies of conservatively managed patients was much greater than would be expected in the United States with 19.3% of the patients with the lowest CCP succumbing to disease. Subset analysis suggests that if the patients with higher risk disease (Gleason score > 7; higher stage) had received definitive treatment (like the current standard in the US) the rate succumbing to disease would likely be substantially better.

The potential usefulness of this test is that it allows physicians to determine which patients with early prostate cancer are candidates for active surveillance or observation and are more likely to have a good outcome without needing to receive definitive treatment.

Analysis of Evidence
(Rationale for Determination)

Level of Evidence
Quality – Moderate
Strength – Moderate
Weight – Limited to moderate

The Prolaris™ assay is covered only when the following clinical conditions are met:

- Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), **and**
- FFPE prostate biopsy specimen with at least 0.5 mm of cancer length, **and**
- Patient Stage as defined by the one of the following:

    - Very Low Risk Disease (T1c **AND** Gleason Score ≤ 6 **AND** PSA ≤ 10 ng/mL **AND** <3 prostate cores with tumor **AND** ≤ 50% cancer in any core **AND** PSA density of < 0.15 ng/mL/g) **OR**
    - Low Risk Disease (T1-T2a **AND** Gleason Score ≤ 6 **AND** PSA ≤ 10 ng/mL), **and**
- Patient has an estimated life expectancy of greater than or equal to 10 years, **and**
- Patient is a candidate for and is considering conservative therapy and yet and would be eligible for definitive therapy (radical prostectomy, radiation therapy or brachytherapy), **and**
- Result will be used to determine treatment between definitive therapy and conservative management, **and**
- Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, **and**
- Test is ordered by a physician certified in the Myriad Prolaris™ Certification and Training Registry (CTR), **and**
- Patient is monitored for disease progression according to established standard of care, **and**
- Physician must report the development of metastasis or prostate cancer deaths in patients not treated definitively who were deemed low risk by the assay.

Certification and Training Registry (CTR) Program

Because of the complicated nature of management decisions utilizing the Prolaris™ assay and the potential for adverse harm to patients if the test is not used appropriately, testing must be furnished only by physicians who are enrolled in a MolDx approved Myriad Prolaris™ CTR program. This serves to assure the appropriate selection of patients, compliance with management decisions and stringent follow up to ensure the benefits of the test outweigh its risks. As part of this requirement Myriad will provide to Palmetto GBA reports every 6 months in a mutually agreed upon format.

The goals of the Myriad Prolaris™ CTR program are as follows:

- To ensure that physicians understand the limitations of the test based on its validation through retrospective and non-U.S. standards of care studies, **and**
- To inform prescribers and patients on the safe-use conditions for Prolaris™, **and**
- Make a good faith effort to identify any safety concerns from the use of the test

Palmetto GBA expects Myriad to:

- Establish and maintain the Prolaris™ Certification and Training Registry (CTR);
- Ensure that healthcare providers who order the Prolaris™ score are registered and certified in the Prolaris™ CTR program and that the Prolaris™ assay is available only through these providers;
- Maintain a secure registry database of Myriad Prolaris™ CTR providers;
- Report utilization data by clinicopathologic staging;
- Immediately report any distant metastases or prostate cancer related deaths in patients who did not receive definitive therapy and were Prolaris™ low risk;
- Share all required data and reports in a HIPAA complaint fashion

Changes/Expectations for Coverage

Expanded coverage to higher risk cohorts (intermediate or high) would require inclusion of the Prolaris™ assay in a widely accepted treatment guideline (such as AUA, NCCN or ASCO), or through successful development of outcome data through published prospective or prospective-retrospective trials showing a favorable clinical outcome (i.e. non-inferiority of non-definitively treated patients).

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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:

81541	ONCOLOGY (PROSTATE), MRNA GENE EXPRESSION PROFILING BY REAL-TIME RT-PCR OF 46 GENES (31 CONTENT AND 15 HOUSEKEEPING), UTILIZING FORMALIN-FIXED PARAFFIN-EMBEDDED TISSUE, ALGORITHM REPORTED AS A DISEASE-SPECIFIC MORTALITY RISK SCORE

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

Group 1 Codes:

ICD-10 Codes	Description
C61	Malignant neoplasm of prostate

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

General Information

Associated Information
N/A

Sources of Information
N/A
Bibliography

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Revision History Information

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
01/01/2018	R5	Replaced CPT code 81479 with 81541.	• Creation of Uniform LCDs With Other MAC Jurisdiction • Revisions Due To CPT/HCPCS Code Changes
12/21/2017	R4	Removed CDD from title.	• Creation of Uniform LCDs With Other MAC Jurisdiction
12/21/2017	R3	Added 21st Century Cures Act Information	• Creation of Uniform LCDs With Other MAC Jurisdiction
11/17/2016	R2	This final LCD, effective 10/15/2015, combines JFA L36349 into the JFB LCD L36350 so that both JFA and JFB contract numbers will have the same final MCD LCD number.	• Creation of Uniform LCDs Within a MAC Jurisdiction
10/15/2015	R1	LCD is revised to add "CDD" (Coverage with Data Development) to the title identifying LCDs which are coverage requiring data development.	• Creation of Uniform LCDs With Other MAC Jurisdiction

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Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) A54592 - Response to Comments: MolDX: Prolaris Prostate Cancer Genomic Assay, L36350

Related National Coverage Documents N/A

Public Version(s) Updated on 04/25/2018 with effective dates 01/01/2018 - N/A Updated on 04/03/2018 with effective dates 12/21/2017 - 12/31/2017 Updated on 12/12/2017 with effective dates 12/21/2017 - N/A Updated on 11/13/2016 with effective dates 11/17/2016 - 12/20/2017 Some older versions have been archived. Please visit the MCD Archive Site to retrieve them. Back to Top

Keywords

- prolaris
- genomic
- assay
- myriad
- MolDX
- malignant
- neoplasm

- prostate
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