

Local Coverage Determination (LCD): MolDX: Prolaris™ Prostate Cancer Genomic Assay (L36348)

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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

LCD Information

Document Information

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For services performed on or after 10/15/2015

LCD Title

MoIDX: Prolaris™ Prostate Cancer Genomic Assay

Revision Effective Date

For services performed on or after 12/01/2019

Proposed LCD in Comment Period

N/A

Revision Ending Date

N/A

Source Proposed LCD

N/A

Retirement Date

N/A

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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.”

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

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	<ul style="list-style-type: none"> • T1c AND • Gleason score ≤ 6 AND • PSA ≤ 10 ng/mL AND 	<ul style="list-style-type: none"> • T1-T2a AND • Gleason score ≤ 6/Gleason grade group 1 AND • PSA ≤ 10 ng/mL 	<ul style="list-style-type: none"> • T2b-T2c OR • Gleason score 3+4= 7/Gleason grade group 2 OR 	<ul style="list-style-type: none"> • T3a OR • Gleason Score 8/Gleason grade group 4 OR • Gleason score

	<ul style="list-style-type: none"> < 3 prostate cores with tumor AND ≤ 50% tumor in any core AND PSA density of < 0.15 ng/mL/g 		<ul style="list-style-type: none"> OR PSA 10-20 ng/mL 	9-10/Gleason grade group 5 OR <ul style="list-style-type: none"> PSA > 20 ng/mL
Treatment Options				
≥ 20 y life expectancy	<ul style="list-style-type: none"> Active Surveillance RT or Brachy RP (± LND) 			
≥ 10 y life expectancy	<ul style="list-style-type: none"> Active Surveillance 	<ul style="list-style-type: none"> Active Surveillance RT or Brachy RP (± LND) 	<ul style="list-style-type: none"> RP (± LND) RT or Brachy ± Adj Horm 	<ul style="list-style-type: none"> RT + Adj Horm RT + Brachy RP + LND ± RT, ADT
< 10 y life expectancy	<ul style="list-style-type: none"> Observation 	<ul style="list-style-type: none"> Observation 	<ul style="list-style-type: none"> RT or Brachy ± Adj Horm Observation 	<ul style="list-style-type: none"> 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 prostatectomy 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 definitive 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 \leq 6 **AND** PSA \leq 10 ng/mL **AND** $<$ 3 prostate cores with tumor **AND** \leq 50% cancer in any core **AND** PSA density of $<$ 0.15 ng/mL/g) **OR**
 - Low Risk Disease (T1-T2a **AND** Gleason Score \leq 6 **AND** PSA \leq 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 prostatectomy, 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).

General Information

Associated Information

N/A

Sources of Information

N/A

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9. Wilt TJ, Brawer MK, Jones KM, et al. Radical prostatectomy versus observation for localized prostate cancer. *N Engl J Med* 2012;367:203-13

Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
12/01/2019	R9	<p>The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.</p> <p>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.</p>	<ul style="list-style-type: none"> Other (The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.)
12/01/2019	R8	<p>12/01/2019: LCD is being revised in order to adhere to CMS requirements per chapter 13, section 13.5.1 of the Program Integrity Manual, to remove all coding from LCDs. There has been no change in coverage with this LCD revision. Regulations regarding billing and coding were removed from the CMS National Coverage Policy section of this LCD and placed in the related Billing and Coding: MolDX: Prolaris™ Prostate Cancer Genomic Assay A57509 article.</p> <p><i>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.</i></p>	<ul style="list-style-type: none"> Provider Education/Guidance
12/01/2019	R7	<p>The following coding and billing guidance is to be used with its associated Local coverage determination.</p> <p>As required by CR 10901, all billing and coding information has been moved to the companion article, this article is linked to the LCD.</p> <p>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</p>	<ul style="list-style-type: none"> Revisions Due To Code Removal
01/01/2018	R6	<p>The link in Bibliography #6 was corrected.</p>	<ul style="list-style-type: none"> Creation of Uniform LCDs With Other MAC Jurisdiction

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
			<ul style="list-style-type: none"> • Typographical Error
01/01/2018	R5	Replaced CPT code 81479 with 81541.	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction • Revisions Due To CPT/HCPCS Code Changes
12/21/2017	R4	Removed CDD from title.	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction
12/21/2017	R3	Added 21st Century Cures Act information	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction
11/17/2016	R2	This final LCD, effective 10/15/2015, combines JEA L36340 into the JEB LCD L36348 so that both JEA and JEB contract numbers will have the same final MCD LCD number.	<ul style="list-style-type: none"> • 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.	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)

A57509 - Billing and Coding: MoIDX: Prolaris™ Prostate Cancer Genomic Assay

A54590 - Response to Comments: MoIDX: Prolaris Prostate Cancer Genomic Assay, L36348

Related National Coverage Documents

N/A

Public Version(s)

Updated on 01/29/2020 with effective dates 12/01/2019 - N/A

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