Local Coverage Determination (LCD): MolDX: Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Disease (L37818)

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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
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LCD Information

Document Information

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LCD Title
MolDX: Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Disease

Proposed LCD in Comment Period
N/A

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DL37818

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

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N/A

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04/11/2019

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05/26/2019

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.

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

CMS On-Line Manual, Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, §§80.0, 80.1.1, 80.2. Clinical Laboratory services.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

This Medicare contractor will provide limited coverage for the Decipher Biopsy Prostate Cancer Classifier Assay (Decipher Biosciences) for men with NCCN low risk and very low risk prostate cancer 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
- Patients with low risk or very low risk as defined by the NCCN as follows:
    - Low Risk:
        - Stage T1 or T2a
        - PSA less than 10 ng/mL
        - Gleason score 6 or less (Grade Group 1) OR
    - Very Low Risk: Stage T1c
        - PSA less than 10 ng/mL
        - Gleason score 6 or less (grade group 1)
        - Not more than two cores with cancer
        - Less than or equal to 50 percent of core involved with cancer
        - PSA density less than 0.15
- 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 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 by active surveillance (AS) and
- Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and
- Patient is monitored for disease progression based on the established standard of care, including at least a repeat biopsy at 1 year

Summary of Evidence

In 2016, over 180,000 men in the US were diagnosed with prostate cancer, which accounts for 10.7% of all new cancer diagnosis. More than 26,000 men will die from this disease representing 4.4% of all cancer deaths. Fortunately, 98.9% of men are surviving at 5 years (SEER).

Many individuals do not need treatment for their prostate cancer because their prognosis is excellent even without treatment. However, physicians and patients struggle to know who can safely be observed versus who needs more aggressive treatment, recognizing that definitive treatment for localized prostate cancer can have lifelong morbidities.

Prostatic needle core biopsy is currently the most reliable standard for diagnosis of prostate cancer, and it is estimated that >800,000 patients undergo prostate biopsy annually in the United States [1]. However, biopsy-based pathological findings and tumor grading do not always accurately predict tumor behavior and patient outcomes due to tumor heterogeneity, biopsy-sampling errors and variations in biopsy interpretation. This can lead to uncertainty in grade assignment and subsequent misclassification of disease severity [2].

Traditionally, despite these limitations, 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**
				Favorable Intermediate subset if:	
Clinico-pathologic 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	• T1-T2a **AND** • Gleason score ≤ 6 **AND** • PSA < 10 ng/mL	• T2b-T2c **OR** • Gleason score 7 **OR** • PSA 10-20 ng/mL	• Predominant Gleason grade 3 (i.e., Gleason score 3+4=7) **AND** • Percent of positive biopsy cores < 50% **AND** • ≤ 1 NCCN intermediate risk factor	• T3a **OR** • Gleason score 8-10 **OR** • PSA > 20 ng/mL

	of < 0.15 ng/mL/g				
Treatment Options					
≥ 20 y life expectancy	• Active surveillance • EBRT or Brachy • RP ± PLND (if predicted probability of lymph node metastasis ≥ 2%)				
≥ 10 y life expectancy	• Active surveillance	• Active surveillance • EBRT or Brachy RP ±PLND (if predicted probability of lymph node metastasis ≥ 2%)	• RP ± PLND (if predicted probability of lymph node metastasis ≥ 2 • **EBRT ± ADT** (4-6 mo) ± brachy or **brachy alone** (low-volume disease) • **Pelvic lymph node irradiation + ADT** (4-6 mo) may be considered	**May be considered for active surveillance**	• EBRT ± ADT (2-3 y) • EBRT + brachy ± ADT (2-3 y) • EBRT + ADT (2-3 y) + docetaxel • Pelvic lymph node irradiation can be considered • RP + PLND
< 10 y life expectancy	• Observation	• Observation	• **EBRT ± ADT** (4-6 mo) **± brachy or brachy alone** (low-volume disease • **Pelvic lymph node irradiation + ADT** (4-6 mo) may be considered • Observation		N/A

Table 1: NCCN 2017 V2 - Localized Prostate Cancer Risk Stratification and Treatment (PSA – Prostate Specific Antigen; EBRT – External Beam Radiation Therapy; RP – Radical Prostatectomy; PLND – Pelvic Lymph Node Dissection; ADT – Androgen Deprivation Therapy)

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 this cure rate. In the PIVOT trial [3] , 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 factors 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.

Recent results from the ProtecT trial [4] of men with primarily low risk prostate cancer randomized to AS or intervention with local therapy also highlight risks for men deferring initial therapy. At a median of 10 years, death from prostate cancer was low irrespective of the treatment assigned. However, roughly 20% of men randomized to AS experienced disease progression to an incurable state (including metastatic disease, locally advanced prostate cancer and need for long term chemical castration), a two-fold increase compared to men treated with local therapy.

These trial findings highlight that more accurate and reliable risk stratification is needed to better inform decision making for physicians and patients choosing between AS and treatment for clinically localized prostate cancer.

Decipher® Biopsy Prostate Cancer Classifier Assay

Test Description

The Decipher® biopsy prostate cancer classifier is a 22-biomarker expression signature measured using oligonucleotide microarray technology, which interrogates 1.4 million RNAs extracted from a formalin-fixed paraffin embedded (FFPE) tissue block of the diagnostic biopsy core (defined by highest Gleason grade). The biomarkers that comprise the Decipher® classifier include cell cycle progression, androgen signaling, cell adhesion, tumor cell motility, migration and immune evasion genes.

Test Performance

Decipher has been evaluated for different clinical endpoints in several clinical cohorts from community and academic-based practice settings. The Decipher test was initially developed using archived FFPE blocks of tumors selected from

621 patients that had undergone a radical prostatectomy (RP) at the Mayo Clinic [5]. The following are non-interventional, blinded, prospectively designed, retrospectively collected studies to validate the performance of the Decipher® assay utilizing biopsies from men diagnosed with localized prostate cancer.

In an initial small study of 57 patients, authors found similar performance of Decipher for predicting short and long-term oncological outcomes when measured in tissue from the initial diagnostic biopsy. The C-index for Decipher for 10-year metastasis risk was much higher at 0.80 (95% CI, 0.63-0.94) than that for Gleason score (0.58; 95% CI, 0.18-0.91) or preoperative PSA (0.57; 95% CI, 0.23-0.89). In this study, Decipher was a significant predictor of 5-year metastasis as well as high-grade disease with a C-index of 0.87 (95% CI, 0.76-0.97) and 0.71 (95% CI, 0.56-0.86), respectively. Using multivariable analysis, Decipher was the only significant predictor of metastasis when adjusting for age, preoperative PSA and GS (Decipher hazard ratio [HR] per 10% increase: 1.72; 95% confidence interval [CI], 1.04–2.83; P=0.02) [6].

A clinical validation study demonstrated the ability of Decipher to predict metastasis as well as prostate cancer specific mortality (PCSM) using needle biopsy specimens. All these patients received primary radiotherapy or radical prostatectomy after initial diagnosis. Decipher reclassified these patients (N=235) to 60% low, 18% intermediate and 23% high risk, and had a C-index of 0.74 (95% confidence interval [CI] 0.63-0.83) compared to 0.60 (95% CI 0.50-0.69) for CAPRA and 0.66 (95% CI 0.53-0.77) for NCCN risk group for predicting metastasis at 5 years post biopsy. In a subset analysis with low and intermediate NCCN risk group patients, Decipher low-, intermediate- and high-risk patients had 0.9%, 7.7% and 26.9% metastasis by 5 years post-biopsy. It was also shown that Decipher was a significant predictor of PCSM (HR 1.57 per 10% increase in score, 95% CI 1.03–2.48, P=0.037) with C-index (95%CI) of 0.73 (0.54-0.85) at 10 years post-biopsy for the PCSM endpoint [7].

In the low-risk population (Gleason score 3+3 or 3+4) of patients treated with RP (n=638), when stratified by Decipher biopsy risk groups, it was observed that 9.7%, 14.9%, 23.5% of men with low, intermediate and high risk Decipher scores, respectively were upgraded or upstaged at RP. Furthermore, for 70 patients with tumor samples from multiple biopsy sites, Decipher showed 85% concordance. These data suggest that, distinct from Gleason grade, the Decipher score does not vary upon the site of the biopsy. With respect to clinical outcomes, in the low-risk population, Decipher high-risk patients had 3.1% PSA failure rate at 3 years from the time of diagnosis and after initial local therapy. For Decipher low and intermediate risk, PSA failure rate by 3 years was 0.9% [8,9].

Analysis from prospective use of the Decipher test showed that among very low and low NCCN risk group patients, 544 (58.7%), 232 (25.0%) and 151 (16.3%) were categorized as Decipher low, intermediate and high-risk, respectively [10,11].

The potential usefulness of this test is that it allows physicians to determine which patients with early prostate cancer are candidates for AS 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 of Evidence – Moderate

Strength of Evidence – Low
Weight of Evidence - Low

Criteria for Coverage

The Decipher Biopsy assay is covered for men with NCCN low risk and very low risk prostate cancer 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
- Patients with low risk or very low risk as defined by the NCCN as follows:
    - Low Risk:
        - Stage T1 or T2a
        - PSA less than 10 ng/mL
        - Gleason score 6 or less (Grade Group 1) OR
    - Very Low Risk: Stage T1c
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        - PSA density less than 0.15
- 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 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 by active surveillance (AS) and
- Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and
- Patient is monitored for disease progression based on the established standard of care, including at least a repeat biopsy at 1 year.

The contractor recognizes that the evidence of clinical utility for Decipher Biopsy in patients with NCCN low risk or very low risk, needle biopsy proven prostate cancer who can be conservatively managed rather than treated with definitive surgery or radiation therapy is limited at the current time. However, this contractor believes that forthcoming prospective clinical studies in these patients will improve patient outcomes and confirm that AS management of patients with low or intermediate scores on Decipher Biopsy is associated with minimal progression. Continued coverage for Decipher Biopsy is dependent on annual review by this contractor of these studies.

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:

CODE	DESCRIPTION
81479	UNLISTED MOLECULAR PATHOLOGY PROCEDURE

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:

N/A

Group 1 Codes:

ICD-10 CODE	DESCRIPTION
C61	Malignant neoplasm of prostate

ICD-10 Codes that DO NOT Support Medical Necessity

N/A

Additional ICD-10 Information

N/A

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
05/27/2019	R1	Revised GenomeDX to Decipher Biosciences.	• Creation of Uniform LCDs With Other MAC Jurisdiction • Other (Revised GenomeDX to Decipher Biosciences.)

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)

A56436 - Response to Comments: MolDX: Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Disease

LCD(s)

DL37818 - MolDX: Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Disease

Related National Coverage Documents

N/A

Public Version(s)

Updated on 05/30/2019 with effective dates 05/27/2019 - N/A

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