Local Coverage Determination (LCD):
MolDX: Decipher® Prostate Cancer Classifier Assay (L36343)

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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

LCD ID

Original Effective Date

L36343

LCD Title	**Revision Effective Date**
MolDX: Decipher® Prostate Cancer Classifier Assay	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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10/14/2015

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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

Coverage Indications, Limitations, and/or Medical Necessity

This Medicare Contractor will provide limited coverage for the Decipher® prostate cancer classifier assay (Decipher Biosciences) when used to determine which patients traditionally considered high risk of recurrence after radical prostectomy (RP) may be closely followed rather than receive post-operative radiation therapy (XRT).

Summary of Evidence

In 2014 the estimated new cases of prostate cancer is 233,000 which represents 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. Physicians and patients struggle to know who can safely be observed versus the subgroup that needs more aggressive treatment to achieve cure.

Traditionally, clinicopathologic characteristics are utilized to determine risk and subsequent treatment. Nearly 50% of men with prostate cancer treated with surgery will have adverse pathology or subsequent PSA rise and are, therefore, considered at increased risk for developing biochemical recurrence (BCR) and ultimately metastatic disease. This represents around 40,000 American men each year. The standard of care for these men is, according to AUA/ASTRO and NCCN clinical practice guidelines, 6-8 weeks of daily postoperative XRT. This recommendation is based on the results of three randomized phase III studies where men who were considered higher risk for BCR were randomized to radiation versus observation. As a group the men who received radiation did better overall, yet approximately 50% of the men in the control group had excellent prognosis without XRT. In the radiation group there was an increase in both acute and chronic adverse events such as rectal complications, urethral strictures and urinary incontinence.

The identification of the subgroup of men who do not need XRT is important. However, prospective studies of outcomes of early prostate cancer (especially where there is a non-intervention arm) will take decades to complete.

Decipher® Prostate Cancer Classifier Assay

Test Description

The Decipher® prostate cancer assay, a 22-biomarker expression signature using oligonucleotide microarray technology, interrogates 1.4 million RNAs extracted from a formalin-fixed paraffin embedded (FFPE) tissue block of the index lesion (defined by highest tumor stage or histological Gleason grade) from the RP specimen. The

biomarkers that comprise the Decipher classifier include cell cycle progression, androgen signaling, cell adhesion, tumor cell motility, migration and immune evasion functions.

Test Performance

The clinical performance of this assay was assessed in several blinded, retrospective, clinical validation studies, enrolling more than 1200 patients. Validation studies included a wide diversity of patients with intermediate or high-risk prostate cancer who underwent RP, many of whom subsequently developed metastatic disease.

Clinical Trials

In a cohort of patients status-post RP with high-risk features (PSA > 20 or GS ≥8) 11% of men received adjuvant XRT and 34% received adjuvant hormone therapy, although it is unclear which patients received salvage RT. In this high-risk population which was largely untreated by adjuvant therapy, the overall risk of metastases was only 7.2% at 10 years. Decipher$^{®}$ classifer (GC) scores of 0.6 group (high risk) had over a 25% risk.

In another study with similar inclusion criteria to the previous study, but with men who had developed BCR. Of the men that developed metastatic disease, only 16% of men received adjuvant XRT (43% received salvage XRT) and 57% of these men received adjuvant androgen deprivation. Despite an imbalance between the non-metastasis and metastasis groups, as would be expected in a retrospective study, the Decipher GC showed that men with a high GC score (≥0.4) had an 8 year risk of metastatic disease of > 50% where as those with a GC score of <0.4 had a risk of metastatic disease of approximately 10%.

In another study with similar inclusion criteria as the first trial, men with pT3b disease were included. In the men eventually dying of metastatic prostate cancer, 14% received adjuvant therapy compared to 34% in the non-cancer death group. The Decipher$^{®}$ GC score showed similar results. Additionally, these authors showed that there was no statistical correlation that adjuvant therapy improved outcomes.

The Decipher GC score on multivariate analysis, has been shown to be the strongest predictor of development of biochemical failure, metastasis or death and outperforms clinicopathologic characteristics currently used in standard practice (including preoperative PSA, Gleason score, surgical findings at time of RP) to determine who is at risk of developing distant metastasis after RP.

The strength of this data is the consistency with which the Decipher GC score predicts metastasis across intermediate or high-risk patients who may or may not have had a BCR. There are heterogeneities in the patients included in the analysis both inside the trials and between trials. While a prospective trial with randomization and treatment based on the Decipher GC score would solve these biases, and recognizing that long-term prospective data would require 10 years or more, Palmetto GBA believes that clinical utility can be extrapolated from these robust retrospective clinical validity trials.

When applying retrospective analysis to prospective treatment there is the fear that the treatment that normally would have been given is altered based on a test result. Consequently, education on the appropriate use of this test and resulting treatment outcomes must be clearly understood by ordering physicians.

Professional Society Opinion

In the 2015 National Comprehensive Cancer Network (NCCN) prostate cancer guidelines, NCCN noted the following: "Men with clinically localized disease could consider use of a tumor-based molecular assay to stratify better risk of adverse pathology at radical prostatectomy or disease-specific mortality after radical prostatectomy."

Analysis of Evidence
(Rationale for Determination)

Level of Evidence

- Quality of Evidence - Moderate
- Strength - Low
- Weight - Low

The Decipher GC assay is covered only when the following clinical conditions are met:

- Patient with prostate cancer who has undergone a RP within the previous 60 months and is being considered for postoperative secondary therapy due to one or more cancer-recurrence risk factors, **and**
- Patient must have achieved initial PSA nadir (defined as PSA at or below 0.2ng/ml) within 120 days of RP surgery, **and**
- Patient must not have any evidence of distant metastasis, and
- Patient must not have received any neo-adjuvant treatment prior to surgery, **and**
- Decipher GC is performed on a patient's RP specimen, **and**
- Patient's surgical pathology report or medical records must have documented presence of adverse pathology:
  - Pathological stage T2 disease with a positive surgical margin, or
  - Pathological stage T3 disease (e.g., extraprostatic extension, seminal vesicle invasion, bladder neck invasion), or
  - Rising PSA after initial PSA nadir, **and**
- Testing has been ordered by a physician who is certified in the Decipher Biosciences Decipher Certification and Training Registry (CTR)

Certification and Training Registry (CTR) Program

Because of the complicated nature of management decisions utilizing the Decipher assay and the potential for missing prostate cancer that could be salvaged with appropriate management at the appropriate time, testing must be furnished only by physicians who are enrolled in a MolDx approved CTR program. The Decipher Biosciences CTR program serves as a control 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 Decipher Biosciences will provide reports every 6 months to Palmetto GBA.

The goals of the Decipher Biosciences Certification and Training Program are as follows:

- To ensure that physicians understand the limitations of the test based on its validation through retrospective and heterogeneous patient populations, and
- To inform prescribers and patients on the safe-use conditions for Decipher, and
- To avoid missing clinically relevant development of metastatic prostate cancer or cancer related death with associated increased morbidity and mortality in Decipher low risk patients

Palmetto GBA expects Decipher Biosciences to:

- Establish and maintain the Decipher Certification and Training Registry (CTR);
- Ensure that healthcare providers who order the Decipher classifier are registered and certified in the Decipher Biosciences Decipher CTR program and that the Decipher classifier assay is available only through these

* providers;
  * Maintain a secure registry database of Decipher Biosciences Decipher CTR providers
  * Immediately report any distant metastases or prostate cancer-related deaths in Decipher GC low risk patients;
  * Apprise Palmetto GBA of all registry or trial results on Decipher on an annual basis;
  * Share all required data and reports in a HIPAA compliant fashion

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General Information

Associated Information

N/A

Sources of Information

N/A

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Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
12/01/2019	R9	The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD. 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	• Other (The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.)
12/01/2019	R8	CMS references are revised.	• Creation of Uniform LCDs With Other MAC

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
		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.	Jurisdiction
12/01/2019	R7	As required by CR 10901, all billing and coding information has been moved to the companion article, this article is linked to the LCD. 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.	• Revisions Due To Code Removal
09/10/2018	R6	GenomeDX is revised to Decipher Biosciences.	• Creation of Uniform LCDs With Other MAC Jurisdiction • Other (GenomeDX is revised to Decipher Biosciences.)
12/21/2017	R5	LCD is revised to delete CDD from the title and under Analysis of Evidence, the following sentence is revised: "Patient must have achieved initial PSA nadir (defined as undetectable PSA at or below 0.2 ng/ml) within 120 days of RP surgery, and…". The following sources were added: CMS Internet-Only Manuals, Publication 100-02, *Medicare Benefit Policy Manual*, Chapter 15, §§80.0, 80.1.1, 80.2. Clinical Laboratory services. CMS Internet-Only Manuals Publication 100-04, *Medicare Claims Processing Manual*, Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes".	• Creation of Uniform LCDs With Other MAC Jurisdiction

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
12/21/2017	R4	Added 21st Century Cures Act Information	• Creation of Uniform LCDs With Other MAC Jurisdiction
11/17/2016	R3	This final LCD, effective 10/15/2015, combines JEA L36341 into the JEB LCD L36343 so that both JEA and JEB contract numbers will have the same final MCD LCD number.	• Creation of Uniform LCDs Within a MAC Jurisdiction
10/15/2015	R2	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
10/15/2015	R1	Removed "No comments were received for comment period ending 03/30/2015" from the Associated Information section.	• Typographical Error

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)
A57623 - Billing and Coding: MolDX: Decipher® Prostate Cancer Classifier Assay
A54631 - Response to Comments: MolDX: Decipher Prostate Cancer Classifier Assay

Related National Coverage Documents

N/A

Public Version(s)

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Updated on 12/05/2019 with effective dates 12/01/2019 - N/A
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Updated on 06/27/2019 with effective dates 09/10/2018 - 11/30/2019
Some older versions have been archived. Please visit the MCD Archive Site to retrieve them.

Keywords

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