Local Coverage Determination (LCD):
MolDX: ConfirmMDx Epigenetic Molecular Assay (L36327)

Links in PDF documents are not guaranteed to work. To follow a web link, please use the MCD Website.

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

Back to Top

LCD Information

Document Information

LCD ID
L36327

LCD Title
MolDX: ConfirmMDx Epigenetic Molecular 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 10/01/2015

Revision Effective Date
For services performed on or after 05/21/2018

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
N/A

Notice Period End Date
N/A

CMS National Coverage Policy
Title XVIII of the Social Security Act (the "Act"), Section 1862(a)(1)(A). This section limits coverage and payment to those items and services that are 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, Section 1833(e). This section prohibits Medicare payment for any claim that lacks the necessary information to process the claim.

42 C.F.R. § 410.32 "Diagnostic X-ray tests, diagnostic laboratory tests, and other diagnostic tests: Condition."

Medicare Internet Online Manual Pub. 100-2 (Medicare Benefit Policy Manual), Chapter 15, Section 80, "Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests."

Medicare Internet Online Manual Pub. 100-4 (Medicare Claims Processing Manual), Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes."

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

Indications and Limitations of Coverage

Noridian will provide limited coverage for the ConfirmMDx epigenetic assay for prostate cancer (MDxHealth, Irvine, CA) to reduce unnecessary repeat prostate biopsies. The MolDX Contractor recognizes that evidence for clinical utility for ConfirmMDx in males with previous negative prostate biopsy who are being considered for repeat biopsy is promising with evidence of some clinical utility at the current time. The MolDX Contractor believes the clinical studies planned will generate sufficient additional data to demonstrate the utility of ConfirmMDx in males with previous negative prostate biopsy who are being considered for repeat biopsy. Continued coverage of ConfirmMDx for males with previous negative prostate biopsy who are being considered for repeat biopsy will be dependent on semi-annual review of interim data, and/or peer-reviewed publications and/or presentations of clinical utility data demonstrating ConfirmMDx for males with previous negative prostate biopsy directs patient management as measured using clinical endpoints in one or more studies.

Summary of Evidence

ConfirmMDx assesses the methylation status of 3 biomarkers (GSTP1, RASSF1, APC) associated with prostate cancer. ConfirmMDx is intended for use in patients with high-risk factors such as elevated/rising prostate-specific antigen (PSA) or abnormal digital rectal examination (DRE), with a negative or non-malignant abnormal histopathology finding (e.g., atypical cell or high grade prostate intraepithelial neoplasia (HGPIN)) in the previous biopsy, and is being considered for repeat biopsy. Several case/control studies in archived biopsy core tissue blocks demonstrated the sensitivity, specificity and high negative predictive value (NPV) of these biomarkers to predict cancer detection in a repeat biopsy procedure. Single biopsy cores, using as little as 20 microns from formalin-fixed, paraffin embedded (FFPE) tissue blocks or sections cut from blocks fixed on glass slides are used in this assay.

The performance of this assay in a large, blinded clinical validation study demonstrated a NPV of 90% for all prostate cancer and 96% for high-grade disease, which is considerably higher than that afforded by standard histopathology review. A mathematically-based budget impact model using the assay in urologic practices to decide upon the need for repeat biopsies reported significant cost and medical resource savings by avoiding unnecessary, invasive biopsies over current standard of care methods. Further logistic regression models using all pertinent risk factors for prostate cancer detection (patient age, serum PSA level, digital rectal exam, histopathological findings on the previous cancer-negative biopsy and the assay) from the clinical validation trial were analyzed to compare various metrics separately and in combination. Assay results and prior histopathology were the strongest predictors of missed cancers and these two measures combined had a higher performance than either alone.

Further analysis demonstrated that the assay test results combined with traditional clinical risk factors improved patient risk stratification and significantly outperformed current risk prediction models such as the Prostate Cancer Prevention Trial Risk Calculator (PCPTRC 2.0) and PSA.

The repeat biopsy rate for patients with an initial negative biopsy was reported to be approximately 40% in the Prostate, Lung, Ovarian and Lung (PLCO) screening trial suggesting that a majority of the patients undergoing repeat biopsies did not have cancer detected. A recently completed field observation study was conducted in 138 patients with negative biopsies and managed by the urologist receiving negative ConfirmMDx for Prostate Cancer assay findings from those patient's tissues. Only 6 of the 138 patients in that series had received a repeat biopsy yielding a 4.5% repeat biopsy rate.

Analysis of Evidence
(Rationale for Determination)

Level of Evidence

Quality of the Evidence: Moderate

Strength of the Evidence: Low

Weight of the Evidence: Low

ConfirmMDx is covered under the following conditions:

1. Males aged 40 to 85 years old that have undergone a previous cancer-negative prostate biopsy within 24 months and are being considered for a repeat biopsy due to persistent or elevated cancer-risk factors, **and**

2. The previous negative prostate biopsy must have collected a minimum of 8 tissue cores (but not have received a saturation biopsy of > 24 tissue cores) and remaining FFPE tissue from all cores is available for testing, **and**

3. Minimum tissue volume criteria of 20 microns of prostate biopsy core tissue is available (40 microns preferable), **and**

4. Previous biopsy histology does not include a prior diagnosis of prostate cancer or cellular atypia suspicious for cancer (but may include the presence of high-grade prostatic intraepithelial neoplasia (HGPIN), proliferative inflammatory atrophy (PIA), or glandular inflammation), **and**

5. Patient is not being managed by active surveillance for low stage prostate cancer, **and**

6. Tissue was extracted using standard patterned biopsy core extraction (and not transurethral resection of the prostate (TURP)), **and**

7. Patient has not been previously tested by ConfirmMDx from the same biopsy samples or similar molecular test.

Back to Top

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:

81551	ONCOLOGY (PROSTATE), PROMOTER METHYLATION PROFILING BY REAL-TIME PCR OF 3 GENES (GSTP1, APC, RASSF1), UTILIZING FORMALIN-FIXED PARAFFIN-EMBEDDED TISSUE, ALGORITHM REPORTED AS A LIKELIHOOD OF PROSTATE CANCER DETECTION ON REPEAT BIOPSY

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

Group 1 Codes:

ICD-10 Codes	Description
D29.1	Benign neoplasm of prostate
N40.0	Benign prostatic hyperplasia without lower urinary tract symptoms
N40.1	Benign prostatic hyperplasia with lower urinary tract symptoms
N40.2	Nodular prostate without lower urinary tract symptoms
N40.3	Nodular prostate with lower urinary tract symptoms

ICD-10 Codes	Description
N41.0	Acute prostatitis
N41.1	Chronic prostatitis
N41.9	Inflammatory disease of prostate, unspecified
N42.81	Prostatodynia syndrome
N42.82	Prostatosis syndrome
N42.83	Cyst of prostate
N42.89	Other specified disorders of prostate
N42.9	Disorder of prostate, unspecified
R97.20	Elevated prostate specific antigen [PSA]

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

Bibliography

References:

1. Ahmed H, et al. Evidence of heavy methylation in the galectin 3 promoter in early stages of prostate adenocarcinoma: development and validation of a methylated marker for early diagnosis of prostate cancer. Transl Oncol. 2009; Aug 18; 2(3): 146-¬-56.
2. Aubry W, et al. Budget impact model: epigenetic assay can help avoid unnecessary repeated prostate biopsies and reduce healthcare spending. American Health Drug and Benefits 2013; Jan/Feb; 6(1): 15-¬-24.
3. Bastian P, et al. Prognostic value of CpG island hypermethylation at PTGS2, RAR-¬-beta, EDNRB, and other gene loci in patients undergoing radical prostatectomy. Eur Uro 2007; Mar; 51(3): 885-¬-74.
4. Devaney J, et al. The epigenetic promise for prostate cancer diagnosis. Cancer Epidemiol Biomarkers Prev 2011; Jan; 20(1): 148-9.
5. Gonzales C, et al. AUA/SUNA white paper on the incidence, prevention and treatment of complications related to prostate needle biopsy. AUA White Paper 2012.
6. Mehorta J, et al. Quantitative, spatial resolution of the epigenetic field effect in prostate cancer. The Prostate 2008; Feb 1; 68(2): 152-60.
7. Steiner I, et al. Gene promoter methylation and its potential relevance in early prostate cancer diagnosis. Pathobiology 2010; Nov; 77(5): 260-¬-6.
8. Stewart G, et al. Clinical utility of an epigenetic assay to detect occult prostate cancer in histopathologically negative biopsies results of the MATLOC study. J Urol 2013; Mar; 189(3): 110-¬-6.
9. Taneja S et al. AUA/optimal techniques of prostate biopsy and specimen handling. AUA White Paper 2013.
10. Trock B, et al. Evaluation of GSTP1 and APC methylation as indicators for repeat biopsy in a high-¬-risk cohort of men with negative initial prostate biopsies. BJU Int. 2013; Jul; 110(1): 56–62.
11. Troyer D, et al. Prostate cancer detected by methylated gene markers in histopathologically cancer-¬-negative tissues from men with subsequent positive biopsies. Cancer Epidemiol Biomarkers Prev 2009; Oct; 18(10): 2717-¬-22.
12. Trujillo L, et al. Markers of field cancerization: Proposed clinical applications in prostate biopsies. Prostate Cancer 2012; 2012:302894.
13. Van Neste L, et al. A tissue biopsy-based epigenetic multiplex PCR assay for prostate cancer detection. BMC Urology 2012; Jun 6; 12:16.

14. Van Neste, et al. The epigenetic promise for prostate cancer diagnosis. The Prostate 2011; Aug 1;72(11): 1248-61.
15. Wojno KJ et al. Reduced rate of repeated prostate biopsies observed in ConfirmMDx clinical utility field study. Am Health Drug Benefit, 2014; May; 7(3):129-34.
16. Zon G, et al. Formamide as a denaturant for bisulfite conversion of genomic DNA: Bisulfite sequencing of the GSTPi and RARβ2 genes of 43 formalin-¬fixed paraffin-¬embedded prostate cancer specimens. Anal Biochem 2009; Sept 15; 392(2): 117-¬-25.
17. Partin A W, et al. Clinical Validation of an Epigenetic Assay to Predict Negative Histopathological Results in Repeat Prostate Biopsies, J Urol 2014, Volume 192, Issue 4, 1081 - 1087.
18. Van Neste L, et al. Risk score predicts high-grade prostate cancer in DNA-methylation positive, histopathologically negative biopsies. The Prostate 76.12 2016: 1078-1087.

Back to Top

Revision History Information

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
05/21/2018	R4	LCD is updated to remove CDD from the title and remove the Pascual trial requirement, delete #8 under the conditions in which Confirm MDx is covered, revise indications and limitations, update for 21st Century Cures Act required fields and add sources 17. Partin and 18. Van Neste.	• Creation of Uniform LCDs With Other MAC Jurisdiction
01/01/2018	R3	2018 Annual CPT/HCPCS Updates: Replaced 81479 with 81551. *01/01/2018 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.* The following ICD-10 codes are added/deleted effective 10/1/16: Added code: R97.20. Deleted code: R97.2	• Creation of Uniform LCDs With Other MAC Jurisdiction • Revisions Due To CPT/HCPCS Code Changes
10/01/2016	R2	N40.0 descriptor was changed in Group 1 from Enlarged prostate without lower urinary tract symptoms to Benign prostatic hyperplasia without lower urinary symptoms. N40.1 descriptor was changed in Group 1 from Enlarged prostate with lower urinary tract symptoms to Benign prostatic hyperplasia with lower urinary tract symptoms.	• Revisions Due To ICD-10-CM Code Changes
10/01/2015	R1	The Part A LCD (L36326) is retired and Part A contract numbers are added to the Part B LCD. 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

Back to Top

Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) A54225 - (MCD Archive Site)

Related National Coverage Documents N/A

Public Version(s) Updated on 05/21/2018 with effective dates 05/21/2018 - N/A Updated on 02/06/2018 with effective dates 01/01/2018 - 05/20/2018 Updated on 09/28/2016 with effective dates 10/01/2016 - 12/31/2017 Some older versions have been archived. Please visit the MCD Archive Site to retrieve them. Back to Top

Keywords

- MDxHealth
- Epigenetic
- MolDX
- 81479
- prostate

Read the **LCD Disclaimer** Back to Top