

Local Coverage Determination (LCD): MolDX: ConfirmMDx Epigenetic Molecular Assay (L36329)

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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

LCD Information

Document Information

LCD ID
L36329

Original Effective Date

For services performed on or after 10/01/2015

LCD Title

Revision Effective Date

MoIDX: ConfirmMDx Epigenetic Molecular Assay

For services performed on or after 11/01/2019

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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Notice Period Start Date

N/A

Notice Period End Date

N/A

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CMS National Coverage Policy

Title XVIII of the Social Security Act, §1862(a)(1)(A). Allows coverage and payment for only those services that are considered to be reasonable and necessary.

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

diagnostic tests: Conditions.

CMS On-Line Manual, 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 16, §50.5 Jurisdiction of Laboratory Claims, 60.1.2 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Noridian will provide limited coverage for the ConfirmMDx epigenetic assay for prostate cancer (MDxHealth, Irvine, CA) to reduce unnecessary repeat prostate biopsies. The MoIDX 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 MoIDX 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.

General Information

Associated Information

N/A

Sources of Information

Bibliography

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.

Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
11/01/2019	R8	<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.)
11/01/2019	R7	<p>11/01/2019: This 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: MoIDX: ConfirmMDx Epigenetic Molecular Assay A57606 article.</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.</p>	<ul style="list-style-type: none"> • Provider Education/Guidance
11/01/2019	R6	<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> <p>Corrected formatting in Bibliography.</p>	<ul style="list-style-type: none"> • Typographical Error • Revisions Due To Code Removal
11/01/2019	R5	<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>	<ul style="list-style-type: none"> • Revisions Due To Code Removal

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.	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction
01/01/2018	R3	<p>2018 Annual CPT/HCPCS Updates: Replaced 81479 with 81551.</p> <p><i>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.</i></p>	<ul style="list-style-type: none"> • Creation of Uniform LCDs With Other MAC Jurisdiction • Revisions Due To CPT/HCPCS Code Changes
10/01/2016	R2	<p>The following ICD-10 codes are added/deleted effective 10/1/16: Added code: R97.20. Deleted code: R97.2</p> <p>N40.0 descriptor was changed in Group 1 from Enlarged prostate without lower urinary tract symptoms to Benign prostatic hyperplasia without lower urinary symptoms.</p> <p>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.</p> <p>The Part A LCD (L36328) is retired and Part A contract numbers are added to the Part B LCD.</p>	<ul style="list-style-type: none"> • Revisions Due To ICD-10-CM Code Changes
10/01/2015	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)

A57606 - Billing and Coding: MoIDX: ConfirmMDx Epigenetic Molecular Assay

A54227

- (MCD Archive Site)

Related National Coverage Documents

N/A

Public Version(s)

Updated on 01/29/2020 with effective dates 11/01/2019 - N/A

Updated on 12/03/2019 with effective dates 11/01/2019 - N/A

Updated on 10/31/2019 with effective dates 11/01/2019 - N/A

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Keywords

N/A