Local Coverage Determination (LCD):
MolDX-CDD: ConfirmMDx Epigenetic Molecular Assay (L35632)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Palmetto GBA	A and B and HHH MAC	11202 - MAC B	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11302 - MAC B	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11402 - MAC B	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11502 - MAC B	J - M	North Carolina

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LCD Information

Document Information

LCD ID
L35632

Original ICD-9 LCD ID
L35368

LCD Title
MolDX-CDD: ConfirmMDx Epigenetic Molecular Assay

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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
Palmetto GBA will provide limited coverage for the ConfirmMDx epigenetic assay for prostate cancer (MDxHealth, Irvine, CA) to reduce unnecessary repeat prostate biopsies. While prospective evidence is currently being generated, retrospective evidence of clinical utility supports the potential value of this diagnostic test and serves as adequate evidence of likely clinical utility to support limited coverage. Palmetto GBA is aware that MDxHealth has initiated the PASCUAL Clinical Trial to prospectively address outcomes to establish clinical utility. Although limited coverage of this assay does support data collection within the PASCUAL trial, participation in the PASCUAL trial is not a prerequisite to the limited coverage. Coverage is limited to providers enrolled in the ConfirmMDx Certification and Training Registry (CTR) program.

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% 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.

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.

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, **and**

8. Testing has been ordered by a physician who is certified in the MolDx approved ConfirmMDx Certification and Training Registry (CTR) program.

Palmetto GBA expects MDxHealth to accrue patients in the PASCUAL trial and expects that, prior to any expansion of the CTR program based on a positive interim analysis result, roughly 50% of all Medicare cases covered under this LCD will be for Medicare patients that are enrolled in the PASCUAL trial. Palmetto GBA expects that preliminary interim analysis of the PASCUAL trial results will become available within 2 years from the beginning of the trial. Under this LCD, if the interim analysis demonstrates a substantially lower re-biospy rate without adverse events, physician participation in the ConfirmMDx CTR program will be expanded, effectively increasing the number of patients tested and covered. If the interim analysis demonstrates poor patient accrual, suggesting limited merit of this assay in clinical practice, or fails to demonstrate a substantially decreased re-biopsy rate, limited coverage will continue until either 1200 patients have been tested or 3 years from the date of this LCD, which ever occurs first. Regardless of the final outcomes, when trial accrual is complete, Palmetto GBA expects peer-reviewed presentation and publication of the PASCUAL trial results. The trial results will be reviewed by Palmetto GBA in the context of a LCD reconsideration. Full coverage and removal of the CTR requirement are expected with favorable trial findings, or non-coverage for unfavorable findings.

Certification and Training Registry (CTR) Program

Because of the complicated nature of management decisions utilizing the ConfirmMDx assay and the potential for missing early prostate cancer, testing must be furnished only by physicians who are enrolled in a MolDx approved CTR program. The ConfirmMDx 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 MDxHealth will provide to Palmetto GBA regular reports every 6 months.

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

- To avoid missing clinically relevant early prostate cancers with associated increased morbidity and mortality,

- To inform prescribers and patients on the safe-use conditions for ConfirmMDx,
- To collect data to inform and manage appropriate utilization and long term safety of patients who were tested but not part of a trial.

Palmetto GBA is aware that MDxHealth has initiated a confirmatory prospective trial (PASCUAL Clinical Trial) addressing the clinical utility and safety of ConfirmMDx. To assure safe use, MDxHealth will ensure that healthcare providers who order ConfirmMDx are registered and certified in the ConfirmMDx CTR program. Coverage for ConfirmMDx testing is available only through these providers. The following criteria must be met in order for a healthcare provider to become certified:

- Must have been trained and certified in the same manner as registered investigators in the ConfirmMDx PASCUAL trial,
- Must manage and follow patients in a similar fashion to those enrolled in the PASCUAL trial,
- Must provide and document patient counseling as to the benefits and risks of ConfirmMDx testing, highlighting the possibility of missing a clinically significant early prostate cancer,
- Must collect and provide, on request to MDxHealth, a limited number of clinical data elements in patients where the test is ordered but the patient is not a participant in a registry or trial where similar outcome data is being collected separately.

Data Element Collection for Patients NOT enrolled in PASCUAL Study:

- General Elements:
    - Total number of tests submitted to Medicare for payment
    - Number of Medicare patients enrolled in ConfirmMDx clinical trial(s), and
    - Number of Medicare tested patients whose data has accrued into the CTR program registry
- Patient Specific Elements (at initial testing):
    - Date of digital rectal examination ("DRE")
    - Date of PSA
    - PSA and DRE findings
    - Dates of previous prostate biopsy(ies), with copies of pathology report preferred
    - ConfirmMDx test results
- Every 6 months:

- Prostate re-biospy to include time (weeks/months) for previous negative biopsy, type of biopsy (trans-rectal vs trans-peritoneal),
- Prostate cancer status (Y/N) to include Gleason score, stage, and PSA at time of detection and treatment(s), when applicable
- Deaths

As part of the Certification and Training registry process, MDxHealth will:

- Maintain a secure database of Confirm MDx CTR providers,
- Monitor to ensure that only ConfirmMDx CTR providers are ordering ConfirmMDx testing.
- Monitor use of the test for patients not enrolled in a clinical trial or outcome focused registry,
- Ensure that CTR providers schedule appropriate follow-up visits following ConfirmMDx testing in accordance with policies based on accepted practice,
- Institute corrective action and prevent a certified provider from enrolling additional patients into the CTR program if the provider fails to come into compliance with the ConfirmMDx CTR program.li>

MDxHealth will develop policies and procedures to provide Palmetto GBA with the required data elements. Palmetto GBA expects MDxHealth to obtain observational data elements on approximately 600 ConfirmMDx test recipients. MDxHealth will also provide representative samples of educational materials, data collection forms, and reporting forms. The reportable data elements will be submitted to Palmetto GBA every 6 months in a mutually accepted format.

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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:
81479 UNLISTED MOLECULAR PATHOLOGY PROCEDURE

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	Enlarged prostate without lower urinary tract symptoms
N40.1	Enlarged prostate with lower urinary tract symptoms
N40.2	Nodular prostate without lower urinary tract symptoms
N40.3	Nodular prostate with lower urinary tract symptoms
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
R97.2	Elevated prostate specific antigen [PSA]

ICD-10 Codes that DO NOT Support Medical Necessity N/A
ICD-10 Additional Information

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General Information

Associated Information
N/A

Sources of Information and Basis for Decision
References:

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Revision History Information

Please note: Most Revision History entries effective on or before 01/24/2013 display with a Revision History Number of "R1" at the bottom of this table. However, there may be LCDs where these entries will display as a separate and distinct row.

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
11/27/2015	R3	Add "-CDD" after MolDX in the LCD title to identify policy as Coverage with Data Development	• Other (Add "-CDD" after MolDX in the LCD title to identify policy as Coverage with Data Development)
10/01/2015	R2	Completed Annual Validation	• Other (Annual Validation)
10/01/2015	R1	Corrected IOM 100-04, Chapter 23, Section 10 to remove ICD-9 reference.	• Other (IOM Update)

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Associated Documents

Attachments N/A

Related Local Coverage Documents N/A

Related National Coverage Documents N/A

Public Version(s) Updated on 11/18/2015 with effective dates 11/27/2015 - N/A Updated on 08/13/2015 with effective dates 10/01/2015 - 11/26/2015 Updated on 06/02/2015 with effective dates 10/01/2015 - N/A Updated on 04/20/2015 with effective dates 10/01/2015 - N/A Back to Top

Keywords

N/A Read the **LCD Disclaimer** Back to Top