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| <b>MEDICAL POLICY</b>  | <b>Prostate: Protein Biomarkers and Genetic Testing<br/>(Medicare Only)</b>   |
| <b>Effective Date: 10/1/2022</b>   | Medical Policy Number: 95   |
| <br>10/1/2022 | Medical Policy Committee Approved Date: 10/16; 12/17; 1/18; 3/18; 8/18; 8/19; 9/19; 11/19; 2/2020; 3/2021; 3/2022; 8/2022; 9/2022 |
| Medical Officer  | Date  |

**See Policy CPT CODE section below for any prior authorization requirements**

**SCOPE:**

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

**APPLIES TO:**

Medicare Only

| <b>MEDICARE POLICY CRITERIA</b>  |           |  |
|--|-----------|--|
| <p>The following Centers for Medicare &amp; Medicaid Service (CMS) guidelines should be utilized for medical necessity coverage determinations. Click the link provided in the table below to access applicable medical necessity criteria. All listed guidelines apply.</p> |           |  |
| Service  | Code(s)   | Medicare Guidelines  |
| <i>4Kscore Assay (developed by OPKO, marketed by BioReference Laboratory; New Jersey)</i>  | CPT 81539 | Select the applicable LCD based on testing location: <ul style="list-style-type: none"> <li>• Testing performed in the states of NC, SC, AL, GA, TN, VA, WV: LCD: MoIDX: 4Kscore Assay (<a href="#">L36763</a>)</li> <li>• Testing performed in the states of AK, ID, OR, WA, UT, AZ, MT, ND, SD, or WY: MoIDX: 4Kscore Assay (<a href="#">L37122</a>)</li> <li>• Testing performed in the states of CA, HI or NV: MoIDX: 4Kscore Assay (<a href="#">L37120</a>)</li> <li>• Testing performed in the states of IL, MN, WI, CT, NY, ME, MA, NH, RI, VT: Biomarker Testing (Prior to Initial Biopsy) for Prostate Cancer Diagnosis (<a href="#">L37733</a>)</li> <li>• Testing performed in the states of NJ, CO, NM, OK, TX, AK, LA, MS, DE, MD, PA: 4Kscore Test Algorithm (<a href="#">L37792</a>)</li> </ul> |

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|   |   | <ul style="list-style-type: none"> <li>• Testing performed in the state of FL: LCD: 4Kscore Test Algorithm (<a href="#">L37798</a>)</li> <li>• Testing performed in the states of KY or OH: LCD: MoIDX: 4Kscore Assay (<a href="#">L36979</a>)</li> </ul> <p>Testing performed in the states of IA, KS, MO, NE, IN, MI: LCD: MoIDX: 4Kscore Assay (<a href="#">L37013</a>)</p>   |
| <p><i>Decipher® Prostate Cancer Classifier Assay (Decipher Biosciences; California)</i></p> <p><i>Oncotype DX® Genomic Prostate Score Assay (California)</i></p> <p><i>Prolaris® Prostate Cancer Genomic Assay (Utah)</i></p> | <p>Varies, but includes CPT 81479, 81541, 81542, or 0047U</p> | <p>For the <b>Decipher® Prostate Cancer Classifier and Oncotype DX® Genomic Prostate Score Assays:</b></p> <ul style="list-style-type: none"> <li>• Apply the LCD for MoIDX: Prostate Cancer Genomic Classifier Assay for Men with Localized Disease (<a href="#">L38339</a>)</li> </ul> <p>For the <b>Prolaris Prostate Cancer Genomic Assay:</b></p> <ul style="list-style-type: none"> <li>• Apply the LCD for MoIDX: Prostate Cancer Genomic Classifier Assay for Men with Localized Disease (<a href="#">L38341</a>)</li> </ul> <p><b>NOTE:</b> While the LCDs above specifically call out the <i>Decipher</i> test by name, they also state <b>other genomic tests may be eligible for coverage as well</b> if evaluated by the MoIDX Program Contractor via the technical assessment (TA) process. Both the <b>Oncotype DX® Genomic Prostate Score Assay</b> and the <b>Prolaris</b> test by Myriad Genetics have completed this requirement and are listed as ‘covered’ tests in the DEX Exchange registry. Thus, the criteria from the above LCDs also apply to these tests as indicated.</p> |
| <p><i>ConfirmMDx Epigenetic Molecular Assay (MDxHealth; Irvine, California)</i></p>   | <p>CPT 81479, 81551</p>                                       | <p>Apply the LCD for MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (<a href="#">L39005</a>) (<i>This test is listed as a potentially covered test in the companion LCA <a href="#">A58718</a> when the member meets the rest of the LCD criteria.</i>)</p>   |
| <p><i>PCA3 Testing</i></p> <p><i>Includes the Progenesa® PCA3 Assay (MetaMark Genetics; Massachusetts or Georgia)</i></p>   | <p>81313</p>  | <p>For PCA3 testing that is specifically the Progenesa® test, apply the following:</p> <ul style="list-style-type: none"> <li>• Testing performed in the states of VA, WV, NC, SC, GA, TN, AL: LCD for MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (<a href="#">L38985</a>) (<i>Use this coverage criteria for testing performed in either location. This test is listed as a potentially covered test in the companion LCA <a href="#">A58724</a> when the member meets the rest of the LCD criteria.</i>)</li> </ul>   |


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|   |           | <p>For PCA3 testing in general that is <b>not</b> specifically the Prega3<sup>®</sup> test, apply the following:</p> <ul style="list-style-type: none"> <li>• Testing performed in the states of IL, MN, WI, CT, NY, ME, MA, NH, RI, VT: LCD for Molecular Pathology Procedures (<a href="#">L35000</a>) (<i>See criteria for PCA3 testing within the LCD, which is the same criteria for CPT 81313 in LCA <a href="#">A56199</a></i>)</li> <li>• Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, and WY: LCD for MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (<a href="#">L39007</a>)</li> </ul> <p>Testing performed in CA and NV: LCD for MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (<a href="#">L39005</a>)</p> |
| <i>Oncotype DX<sup>®</sup> AR-V7 Nucleus Detect Test (California)</i>   | 81479     | LCD: MoIDX: Phenotypic Biomarker Detection from Circulating Tumor Cells ( <a href="#">L38643</a> ) (The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.)  |
| <i>ProMark Risk Score (MetaMark Genetics; Massachusetts or Georgia)</i>   | CPT 81479 | LCD: MoIDX: ProMark Risk Score ( <a href="#">L36665</a> ) ( <i>Use this LCD for testing performed in either location</i> )   |
| <i>ExoDx prostate (also known as ExosomeDx<sup>®</sup>, EPI, or IntelliScore) (Exosome Diagnostics; Massachusetts) (CPT 0005U)</i><br><br><i>Prostate Health Index (PHI or phi) (Beckman Coulter)</i> | Varies    | LCD: Biomarker Testing (Prior to Initial Biopsy) for Prostate Cancer Diagnosis ( <a href="#">L37733</a> )  |
| <i>UroSeq<sup>®</sup> Hereditary DNA Repair Panel (Theranostix, Inc. D/B/A Strand Diagnostics; Indiana)</i>   |           | <p>LCD: MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (<a href="#">L38972</a>) (<i>The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.</i>)</p> <p><b>NOTE:</b> While the UroSeq<sup>®</sup> test may be eligible for coverage, the <i>know error</i><sup>®</sup> system for specimen validity that may also be performed with the UroSeq<sup>®</sup> is <b>not</b> considered medically necessary according to LCA <a href="#">A55172</a>, even if requested in connection to the UroSeq<sup>®</sup> test. Separate coverage or reimbursement will not be allowed for the <i>know error</i><sup>®</sup> system.</p>  |

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| <p><i>RNAinsight™ for ProstateNext® (Ambry Genetics; California) (CPT 0133U)</i></p> <p><i>SelectMDx (MDxHealth; California) (0339U or CPT 81479 if prior to 10/1/2022)</i></p> <p><i>NeoLAB Prostate Liquid Biopsy (NeoGenomics Laboratories, Inc.; California) (CPT 0011M)</i></p> <p><i>Apifyn® Score (Armune BioScience, Inc.; Michigan) (CPT 0021U)</i></p> <p><i>Mi-Prostate score (also known as Michigan Prostate Score or MIPS) (MLabs; Michigan) (CPT 0113U)</i></p> | <p>Varies</p> | <p>These tests are considered <b>not medically necessary</b>, based on Medicare guidelines.</p> <p><i>See “Policy Guidelines” below.</i></p>  |
| <p><i>Prostate Cancer Risk Panel (CPT 0053U) (Mayo Clinic, Mayo Medical Laboratories, headquartered in Minnesota)</i></p> <p><i>EpiScore</i></p> <p><i>miR Sentinel™ Prostate Cancer Test (miR Scientific, LLC.) (CPT 0343U)</i></p>   | <p>Varies</p> | <p>Company medical policy for <a href="#">Prostate: Protein Biomarkers and Genetic Testing (All Lines of Business Except Medicare)</a></p> <p>I. These services are considered <b>not medically necessary</b> for Medicare based on the Company medical policy. <i>Services deemed “investigational” are considered not medically necessary for Medicare Plan members. See <a href="#">Policy Guidelines below.</a></i></p> |

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**POLICY GUIDELINES**

Diagnostic Laboratory Test Jurisdiction

The Company policy *PHA Medicare Medical Policy Development and Application* (MP# 50) describes the Plan’s hierarchy with respect to Medicare medical policy development. In compliance with Medicare guidelines, some LCDs and LCAs used may be for test service areas **outside** of the Company service area. This is because Medicare’s general rule regarding jurisdiction of claims furnished by an independent laboratory is that jurisdiction lies with the A/B MAC (B) (aka, Medicare Contractor) serving the **area in which the laboratory test is performed**.<sup>1</sup>

However, there may be exceptions to this rule. According to Medicare, while jurisdiction for laboratory services normally lies with the carrier serving the performing laboratory service area, there are situations where a regional or national lab chain jurisdiction (e.g., Quest Diagnostics, LabCorp, etc.) lies with a single carrier.<sup>8</sup> Therefore, tests performed by a national laboratory chain may have a single carrier established within the Company medical policies for all laboratory services they perform, regardless of the individual laboratory location. This allows for consistent outcomes for all members who receive the same test by the same lab chain.

Another exception to this rule involves “referring laboratory tests.” This is when one laboratory sends the sample to another laboratory for processing. Under Medicare rules for referred tests, the location of the billing provider determines jurisdiction for claim payment and coverage criteria. Note that also under Medicare rules, only one laboratory is allowed to bill for the services rendered. If the performing laboratory and billing provider both submit a claim, then the performing laboratory’s claim is the claim that would adjudicate according to member benefit.<sup>10-12</sup>

*Medicare’s Molecular Diagnostic (MoIDX) Program Contractor*

While many Medicare contractors (MACs) have adopted guidelines developed and published by the Molecular Diagnostic Services (MoIDX) Program for their service areas, the program is **not** national in scope. MoIDX-related reference materials only apply to genetic and molecular tests performed in the following states: OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY, CA, NV, HI, NC, SC, AL, GA, TN, VA, WV, KY, OH, IA, KS, MO, NE, IN, and MI.<sup>3</sup>

The MoIDX Program was developed by Palmetto GBA in 2011. The MoIDX Contractor performs the following functions<sup>3,4</sup>:

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- Establish clinical utility expectations.
- Complete technical assessments of published test data to determine clinical utility and coverage of individual tests.
- Develop unique test identifiers (Z-codes), adding to the DEX™ register of molecular diagnostic tests to allow for automated claims processing and to track utilization.
- Establish reimbursement.

**Table 1**

Genetic tests performed within a MoIDX service area are required to undergo a technical assessment (TA) review by MoIDX. The LCDs in Table 1 detail this requirement:

|                                   | <b>LOCATION/MEDICARE CONTRACTOR</b>        |                               |                                 |                               |                               |
|-----------------------------------|--|-------------------------------|---------------------------------|-------------------------------|-------------------------------|
|                                   | <b>NORIDIAN J-F</b>                        | <b>NORIDIAN J-E</b>           | <b>PALMETTO GBA J-J AND J-M</b> | <b>WPS J-5 AND J-8</b>        | <b>CGS J-15</b>               |
|                                   | OR, WA, AK, ID, UT, AZ, MT, ND, SD, and WY | CA and NV                     | NC, SC, AL, GA, TN, VA, and WV  | IA, KS, MO, NE, IN, and MI    | KY and OH                     |
| <b>General MoIDX Requirements</b> | <a href="#"><u>L36256</u></a>              | <a href="#"><u>L35160</u></a> | <a href="#"><u>L35025</u></a>   | <a href="#"><u>L36807</u></a> | <a href="#"><u>L36021</u></a> |

The outcome of these TA reviews is maintained in the DEX™ Diagnostics Exchange registry catalog and when possible, the coverage outcome is included within this medical policy to assist with coverage decision-making.

- Tests listed as “not covered” in this catalog have had clinical utility and analytical validity (CU/AV) reviewed and were determined to be **not medically reasonable or necessary** for Medicare under *Social Security Act, §1862(a)(1)(A)*.
- Tests which have **not yet** completed the required TA review are by default also considered to be **not medically reasonable or necessary** for Medicare under *§1862(a)(1)(A)*, based on the requirements found in the LCDs noted in Table 1 above.
- Tests listed as “covered” in this catalog have completed the required TA review and have been determined to be **medically reasonable or necessary** for Medicare under *§1862(a)(1)(A)*; however, this coverage is not automatic, as both of the following must be met:
  - Applicable NCD, LCD, and LCA criteria are met; and,
  - The member has signs/symptoms of a relevant disease or condition.

If a test is not specifically called out in this medical policy, additional research is required to determine coverage.

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**Table 2: Tests relevant to this policy include the following**

*This list only applies to tests which do not have an LCD or LCA specific to that individual test in the Medicare guideline table above. This list was accurate at the time of publication, but it is subject to change at any time by the Medicare MoIDX Program contractor. A “MoIDX TA Review Outcome” of “Covered” does not indicate the test is automatically covered. All relevant criteria from the above Medicare references as applicable to the individual test must still be met.*

| Proprietary Test Name  | Laboratory                                  | MoIDX TA Review Outcome (as found in the DEX™ Diagnostics Exchange registry catalog) |
|--|---|--|
| <b>SelectMDx (CPT 0339U)</b>   | MDxHealth; Irvine (California)              | Not covered  |
| <b>NeoLAB Prostate Liquid Biopsy (CPT 0011M)</b>                                     | NeoGenomics Laboratories, Inc. (California) | Not covered  |
| <b>Apifyn® Score (CPT 0021U)</b>   | Armune BioScience, Inc. (Michigan)          | Not covered (No TA review performed as of most recent policy review date)            |
| <b>Mi-Prostate score (also known as Michigan Prostate Score or MIPS) (CPT 0113U)</b> | MLabs (Michigan)                            | Not covered  |
| <b>UroSeq® Hereditary DNA Repair Panel</b>   | Stand Diagnostics (Indiana)                 | Covered  |
| <b>Oncotype DX® AR-V7 Nucleus Detect Test</b>  | Exact Sciences (California)                 | Covered  |
| <b>Oncotype DX® Genomic Prostate Score Assay</b>                                     | Exact Sciences (California)                 | Covered  |
| <b>RNAinsight™ for ProstateNext® (CPT 0133U)</b>                                     | Ambry Genetics; California                  | Not covered  |

Test coverage or non-coverage positions included in this medical policy were accurate at the time of policy publication, but they are subject to change by the Medicare MoIDX Program contractor at any time. Appeals to dispute non-coverage should include documentation by the MoIDX Contractor which reflects a positive coverage decision (e.g., copy of the MoIDX determination letter).

*Non-MoIDX Service Area Genetic Testing*

Services areas which have **not** adopted MoIDX guidelines include testing performed in the following states: FL, CO, NM, OK, TX, AR, LA, MS, DE, MD, NJ, PA, IL, MN, WI, CT, NY, ME, MA, NH, RI, and VT.

**Table 3**

The LCDs in Table 3 provide general coverage requirements for each jurisdiction area:

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| LOCATION/MEDICARE CONTRACTOR                            |  |  |   |
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| STATE(S)  | MEDICARE CONTRACTOR  | LCD  | COVERAGE REQUIREMENTS   |
| IL, MN, WI,<br>CT, NY, ME,<br>MA, NH, RI,<br>and VT     | <b>National<br/>Government<br/>Services (NGS) J-<br/>6 and J-K</b> | <a href="#"><u>L35000</u></a>              | <p>This LCD requires clinical utility and analytical validity be established, but it doesn't address all tests by name specifically. For panels, this LCD also states, "testing would be covered ONLY for the number of genes or test that are reasonable and necessary to obtain necessary information for therapeutic decision making."</p> <p>In the absence of specific guidance in this LCD, the PHP Company policies for genetic tests provide a peer review of medical literature to evaluate clinical utility/analytical validity. When the biomarkers included in a test do not have proven clinical validity/utility, the test is not medically reasonable or necessary under <i>Social Security Act, §1862(a)(1)(A)</i> for Medicare members.</p>  |
| CO, NM, OK,<br>TX, AR, LA,<br>MI, DE, MD,<br>NJ, and PA | <b>Novitas J-H and<br/>J-L</b>                                     | <a href="#"><u>L35062 /<br/>L35396</u></a> | <p>The LCD L35062 requires clinical utility and analytical validity be established, but it doesn't address all tests by name specifically. Additionally, for multi-biomarker panel test, the LCD L35396 requires evidence to support how "each requested biomarker can be individually contributory."</p> <p>In the absence of specific guidance in these LCDs, the PHP Company policies for genetic tests provide a peer review of medical literature to evaluate clinical utility/analytical validity. When the biomarkers included in a test do not have proven clinical validity/utility, the test is not medically reasonable or necessary under <i>Social Security Act, §1862(a)(1)(A)</i> for Medicare members.</p>  |
| FL  | <b>First Coast<br/>Service Options<br/>J-N</b>                     | <a href="#"><u>L34519</u></a>              | <p>The LCD L34519 requires tests to undergo evaluation to establish clinical utility and analytical validity, based on published peer reviewed medical literature, or be FDA-approved, in order to be eligible for coverage. However, it doesn't address all tests by name specifically. For panels, this LCD also states, "testing would be covered ONLY for the number of genes or test that are reasonable and necessary to establish a diagnosis."</p> <p>In the absence of specific guidance in this LCD, the PHP Company policies for genetic tests provide a peer review of medical literature to evaluate clinical utility/analytical validity. When the biomarkers included in a test do not have proven clinical validity/utility, the test is not medically reasonable or necessary under <i>Social Security Act, §1862(a)(1)(A)</i> for Medicare members.</p> |



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As noted in Table 3, all of the listed LCDs require tests undergo evaluation to establish clinical utility (CU) and analytical validity (AV) in order to be eligible for coverage. However, due to the large number of proprietary tests marketed and available, most genetic tests – particularly panel tests – are not specifically called out by name within an LCD or LCA, nor do LCDs or LCAs provide the outcome for the peer-reviewed CU/AV for most tests.

The Company policy *PHA Medicare Medical Policy Development and Application* (MP# 50) describes the Plan’s hierarchy with respect to Medicare medical policy development. Medicare rules and regulations state that when no NCD, LCD, LCA, or other Medicare coverage guideline exists, Medicare allows Medicare Advantage Organizations (MAOs) to make coverage determinations based on an objective, evidenced-based process. Therefore, in the absence of a specific Medicare policy or reference for a test, Company Commercial medical policy criteria may be applied to panel tests which do not have clinical utility or analytical validity documented within an LCD directly. Tests which are considered “investigational” in a Company Commercial policy will be denied as not medically reasonable or necessary under *Social Security Act, §1862(a)(1)(A)* for Medicare members.

**Table 4: Tests relevant to this policy include the following:**

*Note: This list was accurate at the time of publication, but it is subject to change at any time by a Medicare contractor.*

| Proprietary Test Name                             | Laboratory  | Coverage/Non-coverage Outcome |
|---|---|-------------------------------|
| <b>Prostate Cancer Risk Panel (0053U)</b>         | Mayo Clinic, Mayo Medical Laboratories (Headquartered in Minnesota) | Not Covered                   |
| <b>EpiScore</b>                                   |   | Not Covered                   |
| <b>miR Sentinel™ Prostate Cancer Test (0343U)</b> | miR Scientific, LLC   | Not Covered                   |

**BILLING GUIDELINES**

For applicable billing guidelines, please see related local coverage articles (LCAs):

- Local Coverage Article: Billing and Coding: MoIDX: 4Kscore Assay ([A57337](#))
- Local Coverage Article: Billing and Coding: MoIDX: Prostate Cancer Genomic Classifier Assay for Men with Localized Disease ([A57236](#))
- Local Coverage Article: Billing and Coding: MoIDX: ConfirmMDx Epigenetic Molecular Assay ([A57606](#))
- Local Coverage Article: MoIDX: Oncotype DX Genomic Prostate Score Coding and Billing Article ([A56372](#))
- Local Coverage Article: Billing and Coding: MoIDX: Prostate Cancer Genomic Classifier Assay for Men with Localized Disease ([A57236](#))
- Local Coverage Article: Progensa® PCA3 Assay Billing and Coding guidelines ([A54492](#))

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- Local Coverage Article: Billing and Coding: MoLDX: ProMark Risk Score ([A57609](#))

In accordance with the LCDs and LCAs listed above, CMS has indicated that a number of the assays addressed in the policy be billed with specific codes.

| Assay                              | Code         |
|------------------------------------|--------------|
| 4K score                           | 81539        |
| ConfirmMDx                         | 81479, 81551 |
| Decipher                           | 81479        |
| Oncotype                           | 81479, 0047U |
| PCA3                               | 81313        |
| Prolaris                           | 81479, 81541 |
| ProMark                            | 81479        |
| NeoLAB™                            | 0011M        |
| Mi-Prostate Score (MiPS)           | 0113U        |
| Apifyn®                            | 0021U        |
| ExosomeDx® Prostate (IntelliScore) | 0005U        |
| Prostate Cancer Risk Panel         | 0053U        |
| RNAinsight™ for ProstateNext®      | 0133U        |

## CPT CODES

| Medicare Only                |  |
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| Prior Authorization Required |  |
| 0005U                        | Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score   |
| 0047U                        | Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score                            |
| 81313                        | PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)  |
| 81539                        | Oncology (high-grade prostate cancer), biochemical assay of four proteins (Total PSA, Free PSA, Intact PSA, and human kallikrein-2 [hK2]), utilizing plasma or serum, prognostic algorithm reported as a probability score             |
| 81541                        | Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score |
| 81542                        | Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score  |

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| 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   |
| <p><b>Not Covered</b></p> <p>Based on an LCD or LCA, all codes in this section are <b>non-covered</b> by Medicare or Company policy criteria.</p>  |   |
| 0011M  | Oncology, prostate cancer, mRNA expression assay of 12 genes (10 content and 2 housekeeping), RT-PCR test utilizing blood plasma and/or urine, algorithms to predict high-grade prostate cancer risk  |
| 0021U  | Oncology (prostate), detection of 8 autoantibodies (ARF 6, NKX3-1, 5'-UTR-BMI1, CEP 164, 3'-UTR-Ropporin, Desmocollin, AURKAIP-1, CSNK2A2),   |
| 0053U  | Oncology (prostate cancer), FISH analysis of 4 genes (ASAP1, HDAC9, CHD1 and PTEN), needle biopsy specimen, algorithm reported as probability of higher tumor grade   |
| 0113U  | Oncology (prostate), measurement of PCA3 and TMPRSS2-ERG in urine and PSA in serum following prostatic massage, by RNA amplification and fluorescence-based detection, algorithm reported as risk score   |
| 0133U  | Hereditary prostate cancer–related disorders, targeted mRNA sequence analysis panel (11 genes) (List separately in addition to code for primary procedure)  |
| 0339U  | Oncology (prostate), mRNA expression profiling of HOXC6 and DLX1, reverse transcription polymerase chain reaction (RT-PCR), first-void urine following digital rectal examination, algorithm reported as probability of high-grade cancer ( <i>Used to report the SelectMDx® for Prostate Cancer test by MDxHealth, Inc.</i> )                          |
| 0343U  | Oncology (prostate), exosome-based analysis of 442 small noncoding RNAs (sncRNAs) by quantitative reverse transcription polymerase chain reaction (RT-qPCR), urine, reported as molecular evidence of no-, low-, intermediate- or high-risk of prostate cancer ( <i>Used to report the miR Sentinel™ Prostate Cancer Test by miR Scientific, LLC.</i> ) |
| <p><b>Unlisted Codes</b></p> <p>All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then <b>prior-authorization is required.</b></p> |   |
| 81479  | Unlisted molecular pathology procedure  |
| 81599  | Unlisted multianalyte assay with algorithmic analysis   |
| 84999  | Unlisted chemistry code   |

**INSTRUCTIONS FOR USE**

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to

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| <b>MEDICAL POLICY</b> | <b>Prostate: Protein Biomarkers and Genetic Testing<br/>(Medicare Only)</b> |
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determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days' notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

## REGULATORY STATUS

### Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

## REFERENCES

1. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §50.5 - Jurisdiction of Laboratory Claims; Available at: <https://www.cms.gov/Regulations-andGuidance/Guidance/Manuals/downloads/clm104C16.pdf> [Cited 09/02/2021]
2. Medicare Program Integrity Manual, Chapter 13 – Local Coverage Determinations, §13.5.4 - Reasonable and Necessary Provision in an LCD; Available at: <https://www.cms.gov/Regulationsand-Guidance/Guidance/Manuals/Downloads/pim83c13.pdf> [Cited 09/02/2021]
3. Palmetto GBA MoIDX Manual; Available at: [https://www.palmettogba.com/Palmetto/moldx.Nsf/files/MoIDX\\_Manual.pdf/\\$File/MoIDX\\_Manual.pdf?Open&](https://www.palmettogba.com/Palmetto/moldx.Nsf/files/MoIDX_Manual.pdf/$File/MoIDX_Manual.pdf?Open&) [Cited 09/29/2021]
4. Healthcare Fraud Prevention Partnership (HFPP) White Paper for Genetic Testing Fraud, Waste, and Abuse; Available at: <https://www.cms.gov/hfpp/hfpp-white-papers> [Cited 09/29/2021]
5. Noridian web page for Molecular Diagnostic Services (MoIDX); Last Updated: 9/23/2021; Available at: <https://med.noridianmedicare.com/web/jfb/policies/moldx>
6. Medicare Managed Care Manual, Ch. 4 - Benefits and Beneficiary Protections, §90.4.1 - MACS with Exclusive Jurisdiction over a Medicare Item or Service; Available at: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/mc86c04.pdf>
7. Medicare Claims Processing Manual, Chapter 1 - General Billing Requirements, §10.1.5.4 - Independent Laboratories; Available at: <https://www.cms.gov/Regulations-andGuidance/Guidance/Manuals/Downloads/clm104c01.pdf>
8. Medicare Claims Processing Manual, Chapter 1 - General Billing Requirements, §10.1.5.4 - Independent Laboratories; Available at: <https://www.cms.gov/Regulations-andGuidance/Guidance/Manuals/Downloads/clm104c01.pdf>
9. Noridian LCA for Billing and Coding: MoIDX: Targeted and Comprehensive Genomic Profile Next-Generation Sequencing Testing in Cancer (A56518); Available at: <https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=56518>

**MEDICAL POLICY**

**Prostate: Protein Biomarkers and  
Genetic Testing  
(Medicare Only)**

10. Medicare Claims Processing Manual, Ch. 1 - General Billing Requirements, §10.1.5.4.1 – Cases Involving Referral Laboratory Services; Available at: <https://www.cms.gov/Regulations-andGuidance/Guidance/Manuals/Downloads/clm104c01.pdf>
11. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §40.1 – Laboratories Billing for Referred Tests; Available at: <https://www.cms.gov/regulations-andguidance/guidance/manuals/downloads/clm104c16.pdf>
12. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §50.5.1 - Jurisdiction Of Referral Laboratory Services; Available at: <https://www.cms.gov/regulations-andguidance/guidance/manuals/downloads/clm104c16.pdf>