Medicare Medical Policy

Prostate: Protein Biomarkers and Genetic Testing

MEDICARE MEDICAL POLICY NUMBER: 95

Effective Date: 7/1/2023

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INSTRUCTIONS FOR USE: Company Medicare Medical Policies serve as guidance for the administration of plan benefits and do not constitute medical advice nor a guarantee of coverage. Company Medicare Medical Policies are reviewed annually to guide the coverage or non-coverage decision-making process for services or procedures in accordance with member benefit contracts (otherwise known as Evidence of Coverage or EOCs) and Centers of Medicare and Medicaid Services (CMS) policies, manuals, and other CMS rules and regulations. In the absence of a CMS coverage determination or specific regulation for a requested service, item or procedure, Company policy criteria or applicable utilization management vendor criteria may be applied. These are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. 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.

The Company reserves the right to determine the application of Medicare Medical Policies and make revisions to these policies at any time. Any conflict or variance between the EOC and Company Medical Policy will be resolved in favor of the EOC.

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”).

PRODUCT AND BENEFIT APPLICATION

☒ Medicare Only

MEDICARE COVERAGE CRITERIA

IMPORTANT NOTE: More than one Centers for Medicare and Medicaid Services (CMS) reference may apply to the same health care service, such as when more than one coverage policy is available (e.g., both an NCD and LCD exist). All references listed should be considered for coverage decision-making. The Company uses the most current version of a Medicare reference available at the time of publication; however, these websites are not maintained by the Company, so Medicare references and their corresponding hyperlinks may change at any time. If there is a conflict between the Company Medicare Medical Policy and CMS guidance, the CMS guidance will govern.

Service	Medicare Guidelines
4Kscore Assay (CPT 81539; developed by OPKO, marketed by BioReference Laboratory; New Jersey)	Select the applicable LCD based on testing location: • Testing performed in the states of NC, SC, AL, GA, TN, VA, WV: LCD: MolDX: 4Kscore Assay (L36763) • Testing performed in the states of AK, ID, OR, WA, UT, AZ, MT, ND, SD, or WY: MolDX: 4Kscore Assay (L37122) • Testing performed in the states of CA, HI or NV: MolDX: 4Kscore Assay (L37120) • 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 (L37733) • Testing performed in the states of NJ, CO, NM, OK, TX, AK, LA, MS, DE, MD, PA: 4Kscore Test Algorithm (L37792) • Testing performed in the state of FL: LCD: 4Kscore Test Algorithm (L37798) • Testing performed in the states of KY or OH: LCD: MolDX: 4Kscore Assay (L36979) • Testing performed in the states of IA, KS, MO, NE, IN, MI: LCD: MolDX: 4Kscore Assay (L37013)
Decipher® Prostate Cancer Classifier Assay (CPT 81542; Decipher Biosciences; California) *Oncotype DX® Genomic Prostate Score Assay (CPT 0047U; California)*	For the **Decipher® Prostate Cancer Classifier and Oncotype DX® Genomic Prostate Score Assays**: • Apply the LCD for MolDX: Prostate Cancer Genomic Classifier Assay for Men with Localized Disease (L38339) For the **Prolaris Prostate Cancer Genomic Assay**: • Apply the LCD for MolDX: Prostate Cancer Genomic Classifier Assay for Men with Localized Disease (L38341) **NOTE:** While the LCDs above specifically call out the *Decipher* test by name, they also state **other genomic tests may be eligible for**

Prolaris® Prostate Cancer Genomic Assay (CPT 81541; Utah)	**coverage as well** if evaluated by the MolDX Program Contractor via the technical assessment (TA) process. Both the ***Oncotype DX® Genomic Prostate Score Assay*** and the ***Prolaris*** 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.
ConfirmMDx Epigenetic Molecular Assay (CPT 81551; MDxHealth; Irvine, California)	Apply the LCD for MolDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (L39005) *(This test is listed as a potentially covered test in the companion LCA A58718 when the member meets the rest of the LCD criteria.)*
PCA3 Testing (CPT 81313) *Includes the Progensa® PCA3 Assay (MetaMark Genetics; Massachusetts or Georgia)*	For PCA3 testing that is specifically the Pregensa® test, apply the following: • Testing performed in the states of VA, WV, NC, SC, GA, TN, AL: LCD for MolDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (L38985) *(Use this coverage criteria for testing performed in either location. This test is listed as a potentially covered test in the companion LCA A58724 when the member meets the rest of the LCD criteria.)* For PCA3 testing in general that is **not** specifically the Pregensa® test, apply the following: • Testing performed in the states of IL, MN, WI, CT, NY, ME, MA, NH, RI, VT: LCD for Molecular Pathology Procedures (L35000) *(See criteria for PCA3 testing within the LCD, which is the same criteria for CPT 81313 in LCA A56199)* • Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, and WY: LCD for MolDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (L39007) Testing performed in CA and NV: LCD for MolDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer (L39005)
Oncotype DX® AR-V7 Nucleus Detect Test (CPT 81479; California)	LCD: MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (L38643) (The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.)
ProMark Risk Score (CPT 81479; MetaMark Genetics; Massachusetts or Georgia)	LCD: MoIDX: ProMark Risk Score (L36665) *(Use this LCD for testing performed in either location)*
ExoDx prostate (also known as ExosomeDx®, EPI, or IntelliScore) (Exosome Diagnostics; Massachusetts) (CPT 0005U) *Prostate Health Index (PHI or phi) (Beckman Coulter)*	LCD: Biomarker Testing (Prior to Initial Biopsy) for Prostate Cancer Diagnosis (L37733)

UroSeq® Hereditary DNA Repair Panel (Theranostix, Inc. D/B/A Strand Diagnostics; Indiana)	LCD: MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer (L38972) *(The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.)* **NOTE:** While the UroSeq® test may be eligible for coverage, the *know error®* system for specimen validity that may also be performed with the UroSeq® is **not** considered medically necessary according to LCA A55172, even if requested in connection to the UroSeq® test. Separate coverage or reimbursement will not be allowed for the *know error®* system.
RNAinsight™ for ProstateNext® (Ambry Genetics; California) (CPT 0133U) *SelectMDx (MDxHealth; California) (0339U or CPT 81479 if prior to 10/1/2022)* *NeoLAB Prostate Liquid Biopsy (NeoGenomics Laboratories, Inc.; California) (CPT 0011M)* *Apifiny® Score (Armune BioScience, Inc.; Michigan) (CPT 0021U)* *MyProstateScore (previously known as Michigan Prostate Score [MIPS] or Mi-Prostate score) (Lynx DX; Michigan) (CPT 0113U)* *IsoPSA® (Cleveland Diagnostics, Inc.; Ohio) (CPT 0359U)*	These tests are considered **not medically necessary**, based on Medicare guidelines. *See "Policy Guidelines" below.*
Prostate Cancer Risk Panel (CPT 81479) (Mayo Clinic, Mayo Medical Laboratories, headquartered in Minnesota) *PanGIA Prostate (CPT 0228U) (Genetics Institute of America, Florida)*	Company medical policy for Prostate: Protein Biomarkers and Genetic Testing I. These services are considered **not medically necessary** for Medicare based on the Company medical policy. *See Policy Guidelines below.*

EpiScore *miR Sentinel™ Prostate Cancer Test (miR Scientific, LLC.) (CPT 0343U)*	

IMPORTANT NOTICE: While some services or items may appear medically indicated for an individual, they may also be a direct exclusion of Medicare or the member's benefit plan. Such excluded services or items by Medicare and member EOCs include, but are not limited to, services or procedures considered to be cosmetic, not medical in nature, or those considered not medically reasonable or necessary under *Title XVIII of the Social Security Act, §1862(a)(1)(A).* If there is uncertainty regarding coverage of a service or item, please review the member EOC or submit a pre-service organization determination request. Note that the Medicare Advance Beneficiary Notice of Noncoverage (ABN) form **cannot** be used for Medicare Advantage members. *(Medicare Advance Written Notices of Non-coverage. MLN006266 May 2021)*

POLICY CROSS REFERENCES

None

The full Company portfolio of Medicare Medical Policies is available online and can be accessed here.

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**.[1]

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.[8] 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.[10-12]

Medicare's Molecular Diagnostic (MolDX) Program Contractor

While many Medicare contractors (MACs) have adopted guidelines developed and published by the Molecular Diagnostic Services (MolDX) Program for their service areas, the program is **not** national in scope. MolDX-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.[3]

The MolDX Program was developed by Palmetto GBA in 2011. The MolDX Contractor performs the following functions[3,4]:

- 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: General MolDX Requirements by LCD

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

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

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

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.

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 MolDX Program contractor. A "MolDX 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	MolDX TA Review Outcome (as found in the DEX™ Diagnostics Exchange registry)
SelectMDx (CPT 0339U)	MDxHealth; Irvine (California)	Not covered
NeoLAB Prostate Liquid Biopsy (CPT 0011M)	NeoGenomics Laboratories, Inc. (California)	Not covered
Apifiny® Score (CPT 0021U)	Armune BioScience, Inc. (Michigan)	Not covered *(No TA review performed as of most recent policy review date)*
MyProstateScore (previously known as Michigan Prostate Score [MIPS] or Mi-Prostate score) (CPT 0113U)	Lynx DX (Michigan)	Not covered
UroSeq® Hereditary DNA Repair Panel	Stand Diagnostics (Indiana)	Covered
Oncotype DX® AR-V7 Nucleus Detect Test	Exact Sciences (California)	Covered
Oncotype DX® Genomic Prostate Score Assay	Exact Sciences (California)	Covered
RNAinsight™ for ProstateNext® (CPT 0133U)	Ambry Genetics (California)	Not covered
IsoPSA® (CPT 0349U)	Cleveland Diagnostics, Inc. (Ohio)	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 MolDX Program contractor at any time. Appeals to dispute non-coverage should include documentation by the MolDX Contractor which reflects a positive coverage decision (e.g., copy of the MolDX determination letter).

<u>Summary</u>

Many Medicare contractors (MACs) have adopted guidelines developed and published by the Molecular Diagnostic Services (MolDX) Program for their service area. As called out within relevant LCDs for these

service areas (L36256, L35160, L35025, L36807, L36021), genetic and molecular tests performed within a MolDX service area are required to undergo a technical assessment (TA) review by the MolDX Medicare Contractor, Palmetto GBA. These TA reviews assess clinical utility and analytical validity (CU/AV) to ensure the tests meets requirements for Medicare coverage. The outcome of these TA reviews is maintained in the DEX™ Diagnostics Exchange registry catalog. When possible, the coverage outcome is included within this medical policy to assist with coverage decision-making.

- Tests listed as "not covered" in this registry have had the CU/AV reviewed and were determined to be not medically reasonable or necessary for Medicare under *Social Security Act, §1862(a)(1)(A).*
- Tests not listed at all 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 above.
- Tests listed as "covered" in this registry have completed the required TA review and have been determined to be potentially medically reasonable or necessary for Medicare under *§1862(a)(1)(A)*; however, applicable NCD, LCD, and LCA criteria must still be met, and the member must have signs/symptoms of a relevant disease or condition.

Non-MolDX Service Area Genetic Testing

Services areas which have **not** adopted MolDX 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: Non-MolDX Service Area LCDs

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

STATE(S)	MEDICARE CONTRACTOR	LCD	COVERAGE REQUIREMENTS
IL, MN, WI, CT, NY, ME, MA, NH, RI, and VT	***National Government Services (NGS) J-6 and J-K***	L35000	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." 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 *Social Security Act, §1862(a)(1)(A)* for Medicare members.
CO, NM, OK, TX, AR, LA, MI, DE, MD, NJ, and PA	***Novitas J-H and J-L***	L35062 / L35396	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." 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 *Social Security Act, §1862(a)(1)(A)* for Medicare members.
FL	***First Coast Service Options J-N***	L34519	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." 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 *Social Security Act, §1862(a)(1)(A)* for Medicare members.

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	Company Medical Policy Coverage Position
Prostate Cancer Risk Panel (81479)	Mayo Clinic, Mayo Medical Laboratories (Headquartered in Minnesota)	Not Covered
EpiScore		Not Covered

miR Sentinel™ Prostate Cancer Test (0343U)	miR Scientific, LLC	Not Covered
PanGIA Prostate (CPT 0228U)	Genetics Institute of America	Not Covered

Summary

For service areas which have **not** adopted MolDX guidelines, their applicable LCDs (L35000, L35062 / L35396, L34519) also require that each test have established clinical utility and analytical validity (CU/AV) in order to be eligible for Medicare coverage. Due to the large number of proprietary tests marketed and available, most genetic tests are not specifically called out within an LCD or LCA, nor do LCDs or LCAs provide the outcome for the peer-reviewed CU/AV for most tests. For these service areas, the Plan uses an objective, evidenced-based process to make coverage determinations and the Company medical policy criteria is applied to tests not called out within an LCD directly. See the "Evidence Summary" from the Company Medical Policy for *Prostate: Protein Biomarkers and Genetic Testing* (MP96) for a detailed explanation.

While some tests have demonstrated value in patient management of prostate cancer, not all prostate biomarker or genetic tests meet medical necessity requirements. These non-covered tests include, but may not be limited to, the Prostate Cancer Risk Panel, PanGIA Prostate, EpiScore, and miR Sentinel™ Prostate Cancer Test. These tests are considered not medically reasonable or necessary under *Social Security Act, §1862(a)(1)(A)* for Medicare members.

REGULATORY STATUS

U.S. FOOD & DRUG ADMINISTRATION (FDA)

While clearance by the Food and Drug Administration (FDA) is a prerequisite for Medicare coverage, the 510(k) premarket clearance process does not in itself establish medical necessity. Medicare payment policy is determined by the interaction of numerous requirements, including but not limited to, the availability of a Medicare benefit category and other statutory requirements, coding and pricing guidelines, as well as national and local coverage determinations and clinical evidence.

BILLING GUIDELINES AND CODING

GENERAL

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

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

- Local Coverage Article: Billing and Coding: MolDX: ProMark Risk Score (A57609)

A number of the assays addressed in the policy are to 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
MyProstateScore (previously known as Mi-Prostate Score orMiPS)	0113U
Apifiny®	0021U
ExosomeDx® Prostate (IntelliScore)	0005U
Prostate Cancer Risk Panel	81479
RNAinsight™ for ProstateNext®	0133U
SelectMDx®	0339U
miR Sentinel™ Prostate Cancer	0343U
IsoPSA®	0359U

CODES*		
CPT	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
	0005U	Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score
	0021U	Oncology (prostate), detection of 8 autoantibodies (ARF 6, NKX3-1, 5'-UTR-BMI1, CEP 164, 3'-UTR-Ropporin, Desmocollin, AURKAIP-1, CSNK2A2),
	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
	~~0053U~~	**TERMED 6/30/2023** ~~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)
	0228U	Oncology (prostate), multianalyte molecular profile by photometric detection of macromolecules adsorbed on nanosponge array slides with machine learning, utilizing first morning voided urine, algorithm reported as likelihood of prostate cancer

	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 *(Used to report the SelectMDx® for Prostate Cancer test by MDxHealth, Inc.)*
	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 *(Used to report the miR Sentinel™ Prostate Cancer Test by miR Scientific, LLC.)*
	0359U	Oncology (prostate cancer), analysis of all prostate-specific antigen (PSA) structural isoforms by phase separation and immunoassay, plasma, algorithm reports risk of cancer *(Used to report the IsoPSA® test by Cleveland Diagnostics, Inc.)*
	81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)
	81479	Unlisted molecular pathology procedure
	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
	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
	81599	Unlisted multianalyte assay with algorithmic analysis
	84999	Unlisted chemistry code
HCPCS	None	

***Coding Notes:**

- The code list above is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit. According to Medicare, "presence of a payment amount in the MPFS and the Medicare physician fee schedule database (MPFSDB) does not imply that CMS has determined that the service may be covered by Medicare." The issuance of a CPT or HCPCS code or the provision of a payment or fee amount by Medicare does **not** make a procedure medically reasonable or necessary or a covered benefit by Medicare. *(Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician's Fee Schedule, A. Physician's Services)*
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

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 MolDX Manual; Available at: https://www.palmettogba.com/Palmetto/moldx.Nsf/files/MolDX_Manual.pdf/$File/MolDX_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 (MolDX); 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:
7. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/mc86c04.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
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POLICY REVISION HISTORY

DATE	REVISION SUMMARY
1/2023	Q1 2023 code updates (converted to new format 2/2023)
6/2023	Annual review. Moved 0228U from a different policy to this policy
7/2023	Q3 2023 code updates