

Medicare Advantage Medical Policy



Prostate Cancer Early Detection: Biomarkers Prior to Biopsy – Medicare Advantage

Medicare Advantage Plan

- ☒ Medicare Plus BlueSM
- ☒ BCN AdvantageSM

UM Committee Approval Date: 7/15/2026

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Description

Prostate biomarker testing prior to biopsy refers to the use of laboratory tests that measure specific biological markers in blood, urine, or other specimens to estimate an individual's risk of having clinically significant prostate cancer before a prostate biopsy is performed. These tests are intended to supplement traditional risk assessment tools, such as prostate-specific antigen (PSA) testing, digital rectal examination (DRE), patient age, family history, and other clinical factors. The results may help identify individuals who are more likely to benefit from biopsy and those who may be at lower risk, potentially reducing unnecessary biopsies and associated complications.

Related Medical Coverage Policies

- Computer-Aided Evaluation as an Adjunct to Magnetic Resonance Imaging for Prostate Cancer – Medicare Advantage
 - Gene Expression Profile Analysis for Risk Stratification for Prostate Cancer Management – Medicare Advantage
 - Germline and Somatic Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment in Prostate Cancer (BRCA1/2, Homologous Recombination Repair Gene Alterations) – Medicare Advantage
 - Magnetic Resonance Imaging – Targeted Biopsy of the Prostate – Medicare Advantage
 - Saturation Biopsy for Diagnosis and Staging of Prostate Cancer – Medicare Advantage
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Policy Guidelines

Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network of Michigan (BCN) adhere to guidance from the Centers for Medicare and Medicaid Services (CMS), including when performing organization determinations for Medicare Advantage plan members. CMS Medicare statutes, regulations, manuals, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and other sub-regulatory

guidance provide the clinical guidelines for coverage determinations, payment integrity functions, and all other uses by CMS regulations. When CMS Medicare guidance is silent, incomplete, or insufficient, CMS permits BCBSM/BCN to utilize “internal coverage criteria”, such as independent criteria, health plan policy research, LCD/LCAs outside the services area or research from independent medical research repositories (i.e., Hayes) for coverage policies consistent with 42 CFR § 422.101. BCBSM/BCN internal medical coverage policies are developed and based on current evidence in widely accepted treatment guidelines or clinical literature; in addition, they address how clinical benefits may or may not outweigh member harm.

Clinical review follows guidance provided in the BCBSM Medicare Advantage Coverage Determination Hierarchy policy, which may be found at <https://www.bcbsm.com/providers/mpradmin/> by entering the policy name.

Coverage Guidance

To ensure consistency with coverage guidance, the Medicare statutes, regulations, coverage manuals, NCD, LCD, and LCA should be reviewed and applied first. BCBSM/BCN internal coverage criteria should only be applied when CMS guidance is silent, incomplete, or insufficient for a code.

Apart from durable medical equipment (DME), Medicare Administrative Contractor (MAC) jurisdiction for the purpose of clinical determination is based upon place of service. The place of service for laboratory testing is defined as the geographic location of the reference laboratory. Non-jurisdictional LCD/LCAs may not be utilized for a determination unless they have been specifically identified as internal coverage criteria by the policy. Alternatively, jurisdiction for DME MAC is determined by the member place of residence. Please see CMS Medicare Administrative Contractors (MAC) table for state MAC assignments below.

CMS Guidance	Additional Guidance
National Coverage Determinations 190.31 - Prostate Specific Antigen Local Coverage Determinations and Articles WPS L36807, A57772 – MoIDX: Molecular Diagnostic Tests (MDT)* L38429, A57100 – MoIDX: Repeat Germline Testing* L39042, A58759 – MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer* A59700 – MoIDX: Defining panel services in MoIDX* CGS L36021, A56973 – MoIDX: Molecular Diagnostic Tests (MDT)* L38288, A57141 – MoIDX: Repeat Germline Testing* L38997, A58713 – MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer*	BCBSM/BCN will follow CMS guidance as the primary source for coverage determinations. However, in instances where CMS guidance is silent, incomplete, or insufficient for a particular code, BCBSM/BCN internal coverage criteria will be applied to ensure consistent and informed decision-making. In such cases, please refer to the relevant BCBSM/BCN policy for guidance: <i>Prostate Cancer Early Detection: Biomarkers Prior to Biopsy</i> To access this policy, please visit the BCBSM Medical Policy Router Search page at https://www.bcbsm.com/providers/mpradmin/ and enter the policy name in the search field.

CMS Guidance	Additional Guidance
L39284, A59066 – Prostate Cancer Detection with IsoPSA™ First Coast L34519, A57451 – Molecular Pathology Procedures A58918 – Molecular Pathology and Genetic Testing L39367, A59123 – Genetic Testing for Oncology L37798, A56287 – 4Kscore Test Algorithm Noridian JE & JF L35160, A57526 – MoIDX: Molecular Diagnostic Tests (MDT)* L38351, A57331 – MoIDX: Repeat Germline Testing* L39005, A58718 – MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer* A59685 MoIDX: Defining panel services in MoIDX* Novitas L35062, A56541 – Biomarkers Overview A58917 – Molecular Pathology and Genetic Testing L35396, A52986 – Biomarkers for Oncology A59125 – Genetic Testing in Oncology: Specific Tests L37792, A56653 – 4Kscore Test Algorithm Palmetto L35025, A56853 – MoIDX: Molecular Diagnostic Tests (MDT)* L38274, A58017 – MoIDX: Repeat Germline Testing* L38985, A58700 – MoIDX: Molecular Biomarkers to Risk-Stratify Patients at Increased Risk for Prostate Cancer* Wellpoint Federal L35000, A56199 – Molecular Pathology Procedures A56609 – Biomarker Testing for Prostate Cancer Diagnosis	

Code	Description
81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants, comparative genomic hybridization (CGH) microarray analysis
81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (e.g., prostate cancer) [Progenisa® PCA3 Assay, Hologic]

Code	Description
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 [4Kscore] [4Kscore®]
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 [ConfirmMDx]
81599	Unlisted multianalyte assay with algorithmic analysis
84153	Prostate specific antigen (PSA); total
84154	Prostate specific antigen (PSA); free [percent-free PSA]
86316	Immunoassay for tumor antigen, other antigen, quantitative (e.g., CA 50, 72-4, 549), each [e.g., Prostate Health Index (PHI), phi]
0005U	Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score [ExosomeDx® Prostate (IntelliScore), Exosome Diagnostics, Inc. MA, CA, TX]
0021U	Oncology (prostate), detection of 8 autoantibodies (ARF 6, NKX3-1, 5'-UTR-BMI1, CEP 164, 3'-UTR-Ropporin, Desmocollin, AURKAIP-1, CSNK2A2), multiplexed immunoassay and flow cytometry serum, algorithm reported as risk score [Apify®], Armune BioScience, Inc. MI]
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 [PanGIA Prostate, Genetics Institute of America, Entopsis, LLC, FL]
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 [SelectMDx® for Prostate Cancer, MDxHealth®, Inc, MDxHealth®, Inc. CA]
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 [miR Sentinel™ Prostate Cancer Test, miR Scientific, LLC, NJ]
0359U	Oncology (prostate cancer), analysis of all prostate-specific antigen (PSA) structural isoforms by phase separation and immunoassay, plasma, algorithm reports risk of cancer [IsoPSA®, Cleveland Diagnostics, Inc, OH]
0403U	Oncology (prostate), mRNA, gene expression profiling of 18 genes, first-catch post-digital rectal examination urine (or processed first-catch urine), algorithm reported as percentage of likelihood of detecting clinically significant prostate cancer [MyProstateScore 2.0, LynxDX, MI]
0424U	Oncology (prostate), exosome-based analysis of 53 small noncoding RNAs (sncRNAs) by quantitative reverse transcription polymerase chain reaction (RT qPCR), urine, reported as no molecular evidence, low-, moderate- or elevated-risk of prostate cancer [miR Sentinel™ Prostate Cancer Test, miR Scientific®, LLC. NJ]
0433U	Oncology (prostate), 5 DNA regulatory markers by quantitative PCR, whole blood, algorithm, including prostate-specific antigen, reported as likelihood of cancer [EpiSwitch® Prostate Screening Test (PSE), Oxford BioDynamics Inc. UK]
0495U	Oncology (prostate), analysis of circulating plasma proteins (tPSA, KLK2, PSP94, and GDF15), germline polygenic risk score (60 variants), clinical information (age, family history of prostate cancer, prior negative prostate biopsy), algorithm reported as risk of detecting clinically significant prostate cancer [Stockholm3, BioAgilytix Diagnostics, MA]

Code	Description
0572U	Oncology (prostate), high-throughput telomere length quantification by FISH, whole blood, diagnostic algorithm reported as risk of prostate cancer [ProsTAV®, Life Length S.L., FL, PA, TX]
0591U	Oncology (prostate cancer), biochemical analysis of 3 proteins (total PSA, free PSA, and HE4), plasma, serum, prognostic algorithm incorporating 3 proteins and digital rectal examination, results reported as a probability score for clinically significant prostate cancer [MiCheck® Prostate, Minomic®, Inc. MD]
0609U	Oncology (prostate), immunoassay for total prostate-specific antigen (PSA) and free PSA, serum or plasma, combined with clinical features, algorithm reported as a probability score for clinically significant prostate cancer [ClarityDX Prostate, Protean BioDiagnostics, Nanostics Inc. FL]

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* **CMS MoIDX Program:** The MoIDX Program, administered by Palmetto GBA, is a Medicare Molecular Diagnostic Program that aims to identify and establish coverage and reimbursement for molecular diagnostic tests. This program is implemented by several Medicare Administrative Contractors (MACs), including **WPS, CGS, Noridian, and Palmetto**.

The MoIDX Program evaluates genetic and proteomic tests to determine their analytical and clinical validity (AV/CV) and clinical utility (CU), ensuring that each test meets Medicare criteria.

The program's coverage determinations are maintained in the DEX™ Diagnostic Exchange registry. Dex Diagnostic Exchange Registry Coverage Determinations:

1. Not Covered: Not covered tests in the Dex Registry have undergone a review of their clinical utility and analytical validity and have been determined to not meet the requirements for medical necessity under Section 1862(a)(1)(A) of the Social Security Act. As a result, they are not considered medically reasonable or necessary for Medicare coverage.
2. No Determinations: Tests that have not completed the required technical assessment (TA) review are, by default, also considered not medically reasonable or necessary for Medicare under Section 1862(a)(1)(A) until the review is completed. The MoIDX Program does not provide coverage for tests provided with dates of services prior to the effective date of approval.
3. Covered: Covered Tests in Dex Registry have completed the required TA review and have been determined to be medically reasonable and necessary for Medicare under Section 1862(a)(1)(A). However, coverage is not automatic and is subject to the following conditions:
 - a. The test must meet the applicable criteria outlined in NCDs, LCDs, and LCAs; and
 - b. The patient must exhibit signs or symptoms of a relevant disease or condition, making the test medically necessary for their care.

For specific coding and billing information on covered and excluded tests, please refer to the MoIDX website at <https://www.palmettogba.com/MoIDX>. This website provides up-to-date information on the program's coverage determinations and guidelines.

NOTE: Per § 2.3.3. of the Molecular Diagnostic Program [MoIDX®] Manual, the MoIDX Program does not provide coverage for tests that have not been reviewed and approved through the MoIDX process or for tests provided with dates of services prior to the effective date of approval. For additional information regarding what tests will fall into a Medicare benefit category or which tests are statutory excluded (e.g., predictive, prenatal, and carrier testing and tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law) please refer to <https://www.palmettogba.com/palmetto/moldxv2.nsf/DID/DPR5GEM991>

The above information is current as of the review date for this policy. However, the coverage issues and policies maintained by CMS are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document.

Please refer to the Medicare Coverage Database website at <https://www.cms.gov/medicare-coverage-database/search.aspx> for the most current applicable NCD, LCD, LCA, and CMS Online Manual System Transmittals. For any code associated with a product or service determined to be noncovered by policy (either CMS or health plan policy if CMS is silent) medical record review, including prior authorization, will not be required.

CMS Medicare Administrative Contractors (MAC) Jurisdictions Guidance

Part A and Part B MAC Jurisdictions	
Wisconsin Physicians Service Insurance Corporation (WPS)	IA, IN, KS, MI, MO, NE
CGS Administrators, LLC	KY, OH
First Coast Service Options, Inc	FL, PR, US VI
Noridian Healthcare Solutions, LLC Jurisdiction JE	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
Noridian Healthcare Solutions, LLC Jurisdiction JF	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
Novitas Solutions Inc.	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX
Palmetto GBA	AL, GA, TN, NC, SC, VA, WV
Wellpoint Federal - Previously known as National Government Services, Inc. (NGS)	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI
DME MAC Jurisdictions	
CGS Administrators, LLC, Jurisdictions JB and JC	AL, AR, CO, FL, GA, IL, IN, KY, LA, MI, MN, MS, NM, NC, OH, OK, Puerto Rico, SC, TN, TX, VA, US Virgin Islands, WI, WV
Noridian Healthcare Solutions, LLC, Jurisdictions JA and JD	AK, American Samoa, AZ, CA, CT, DE, DC, Guam, HI, ID, IA, KS, MA, MD, ME, MO, MT, ND, NE, NH, NJ, NV, NY, Northern Mariana Islands, OR, PA, RI, SD, UT, VT, WA, WY

Important Reminder

BCBSM and BCN follow CMS Medicare coverage guidance to limit coverage to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member. Medicare Advantage Medical Policies list the criteria BCBSM and BCN use to decide which medical services are considered “reasonable and necessary” when Medicare coverage rules are not fully developed, or as otherwise permitted by CMS Medicare regulations. Individual member benefit plan documents, such as the Evidence of Coverage and Annual Notice of Change, as well as

applicable laws govern benefit coverage, including any inclusion, exclusion, and/or other restrictions.

Medicare Advantage Medical policies are created when permitted by CMS Medicare regulations, reviewed regularly, and may be revised periodically. BCBSM/BCN Medical Policies are proprietary and should not be copied or disseminated without the express, prior written approval of BCBSM. All providers are required to review applicable BCBSM reimbursement policies prior to claim submission and bill for covered services in accordance with those policies. Additionally, providers contracted with BCBSM or BCN's Medicare Advantage network(s) should review the provider manual for any additional claim submission requirements. Providers not contracted with BCBSM or BCN's Medicare Advantage network may be required to submit documentation to BCBSM, BCN, or its delegated entity supporting billed claims, including but not limited to applicable medical records.

Note: U.S. Food and Drug Administration (FDA) approval for a specific indication or the issuance of a CPT code is not sufficient for a procedure to be considered medically reasonable and necessary. Similarly, the presence of a procedure/device code or payment amount for the service in the Medicare fee schedule does not necessarily indicate coverage. If a service is deemed not reasonable and necessary, to treat illness or injury for any reason (including lack of safety and efficacy because it is an experimental procedure, etc.), the procedure is considered not covered.

Disclaimer: This medical policy is not an authorization, certification, explanation of benefits, or a contract for the services, devices, or drugs that is referenced in the medical policy. Medical policies do not constitute medical advice and do not guarantee any results or outcomes or guarantee payment. The medical policy is not intended to replace independent medical judgment for the treatment of individuals. Treating physicians and health care providers are solely responsible for determining what care to provide for their patients. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test, or procedure over another.

Pursuant to Section 1557 and Section 504, Blue Cross does not discriminate on the basis of race, color, national origin, age, disability, or sex (including sex characteristics, intersex traits; pregnancy or related conditions; sexual orientation; gender identity, and sex stereotypes). This includes our rules, benefit designs and medical policies.

BCBSM/BCN Medicare Advantage Policy History

Policy Effective Date	UM Committee Approval Date	Comments
08/17/2024	07/17/2024	Medicare Advantage policy established
08/16/2025	07/16/2025	Annual Review or Off-Cycle Review: MA Policy Foundational Language updated. Adopted JUMP policy Updates
02/28/2026	01/28/2026	Off-cycle review, code updates. Adopted JUMP policy updates
08/15/2026	07/15/2026	Annual Review: Reformatted guidance and code tables. Adopted JUMP policy updates including adding code 0609U. Revised policy description and updated CMS guidance.