Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 1/1/25**
(See policy history boxes for previous effective dates)

Title: Prostate Cancer Early Detection: Biomarkers Prior to Biopsy

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Description/Background

Prostate Cancer

Prostate cancer is the most common cancer, and the second most cause of cancer death in men. Prostate cancer is a complex, heterogeneous disease, ranging from microscopic tumors unlikely to be life-threatening to aggressive tumors that can metastasize, leading to morbidity or death. Early localized disease can usually be cured with surgery and radiotherapy, although active surveillance may be adopted in men whose cancer is unlikely to cause major health problems during their lifespan or for whom the treatment might be dangerous. In Individuals with inoperable or metastatic disease, treatment consists of hormonal therapy and possibly chemotherapy. The lifetime risk of being diagnosed with prostate cancer for men in the U.S. is approximately 16%, while the risk of dying of prostate cancer is 3%.[1] African-American men have the highest prostate cancer risk in the U.S.; the incidence of prostate cancer is about 60% higher and the mortality rate is more than 2 to 3 times greater than that of White men.[2] Autopsy results have suggested that about 30% of men age 55 and 60% of men age 80 who die of other causes have incidental prostate cancer[3], indicating that many cases of cancer are unlikely to pose a threat during a man's life expectancy.

Grading

The most widely used grading scheme for prostate cancer is the Gleason system.[4] It is an architectural grading system ranging from 1 (well-differentiated) to 5 (undifferentiated); the score is the sum of the primary and secondary patterns. A Gleason score of 6 or less is low-grade prostate cancer that usually grows slowly; 7 is an intermediate grade; 8 to 10 is high-grade cancer that grows more quickly. A revised prostate cancer grading system has been adopted by the National Cancer Institute and the World Health Organization.[5] A cross-walk of these grading systems is shown in Table 1. A narrative of Prostate Cancer Grading System is featured in NCCN Guidelines 2.2024 Prostate Cancer: Early Detection.

Table 1. Prostate Cancer Grading System

Grade Group	Gleason Score (Primary and Secondary Pattern)	Cells
1	6 or less	Well-differentiated (low grade)
2	7 (3 + 4)	Moderately differentiated (moderate grade)
3	7 (4 + 3)	Poorly differentiated (high grade)
4	8	Undifferentiated (high grade)
5	9-10	Undifferentiated (high grade)

Numerous genetic alterations associated with the development or progression of prostate cancer have been described These molecular markers are used to identify the selection of men who should undergo an initial prostate biopsy or a repeat biopsy after an initial negative biopsy.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. Tests must be licensed under the Clinical Laboratory Improvement Amendments for high-complexity testing. The following laboratories are certified under the CLIA: BioReference Laboratories and GenPath Diagnostics (subsidiaries of OPKO Health; 4Kscore®), ARUP Laboratories, Mayo Medical Laboratories, LabCorp, BioVantra, others Prostate Cancer Antigen (PCA3 assay), Clinical Research Laboratory (Prostate Core Mitomic Test™), MDx Health (Select MDx®, ConfirmMDx®), and Innovative Diagnostics (phi™), and ExoDx® Prostate (Exosome Diagnostics). To date, the U.S. Food and Drug Administration (FDA) has chosen not to require any regulatory review of these tests.

In February 2012, the Progensa® PCA3 Assay (Gen-Probe; now Hologic, Marlborough, MA) was approved by FDA through the premarket approval process. The Progensa PCA3 assay has been approved by FDA to aid in the decision for repeat biopsy in men 50 years or older who have had one or more negative prostate biopsies and for whom a repeat biopsy would be recommended based on the current standard of care. The Progensa PCA3 assay should not be used for men with atypical small acinar proliferation on their most recent biopsy. FDA product code: OYM.

In June 2012, proPSA, a blood test used to calculate the Prostate Health Index (phi; Beckman Coulter, Brea, CA) was approved by FDA through the premarket approval process. The phi test is indicated as an aid in distinguishing prostate cancer from benign prostatic condition in men ages 50 and older with prostate-specific antigen levels of 4 to 10 ng/mL and with digital rectal exam findings that are not suspicious. According to the manufacturer, the test reduces the number of prostate biopsies. FDA product code: OYA.

Medical Policy Statement

For the purpose of early detection of prostate cancer, testing of genetic and protein biomarkers prior to an initial or repeat biopsy is considered established when criteria are met.

Other biomarker genetic testing for prostate cancer that does not meet our inclusionary criteria is considered experimental/investigational. Results of this testing has not been shown to improve clinical health outcomes.

Inclusionary and Exclusionary Guidelines

It is expected that the FDA or manufacturer test guidelines will be followed.

Please refer to NCCN Guidelines® 2.2024 Prostate Cancer: Early Detection. This information is also in the supplemental section for the list of updated biomarkers.

Inclusions:

A. Genetic and protein biomarker tests for early detection of prostate cancer are established prior to an **initial** biopsy:
   - In individuals over 45 years of age who are considered average risk, AND
     - Have a PSA level > 3 ng/mL and have been evaluated for benign prostate disease OR
     - Have a very suspicious digital rectal examination (DRE)

   OR
   - In individuals over 40 years of age who:
     - Are Black/African American, OR Have germline mutations that increase the risk of prostate cancer, OR Who have a family history of prostate cancer

     AND
     - Have a PSA level > 3 ng/mL and have been evaluated for benign prostate disease OR
     - Have a very suspicious digital rectal examination (DRE), AND

Biomarker tests that improve the specificity of cancer detection include: percent-free PSA, Prostate Health Index (PHI), SelectMDx®, 4Kscore®, ExoDx™ (EPI), MyProstateScore2.0 (MPS2), and IsoPSA.

B. Genetic and protein biomarker tests for early detection of prostate cancer are established prior to a **repeat** biopsy:
   - In individuals who had an initial biopsy with results of:
     - Atypia, suspicious for cancer, OR
     - High-grade prostatic intraepithelial neoplasia (PIN), OR
     - Have a family history of prostate cancer

Biomarker tests that improve specificity in the post-biopsy setting include: percent-free PSA, Prostate Health Index (PHI), 4Kscore®, Progensa® PCA3, ConfirmMDx®, MyProstateScore2.0 (MPS), IsoPSA, and ExoDx™ (EPI).

Exclusions:

- **Multiple biomarker testing for same indications**
- Biomarker tests are not covered if criteria above are not met. (this is not an all-inclusive biomarker list)
  - Mitochondrial DNA mutation testing (eg, Prostate Core Mitomic Test™)
  - PanGIA Prostate
  - EpiSwitch® Prostate Screening Test
  - miR Sentinel™ Prostate Cancer Test
  - Stockholm3

Biomarker testing is not expected to be performed more frequently than every 12 months and can only be performed when there is a clinical change. (Ex: significant PSA change)

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

81313	81539	81551	84153	84154
86316	0005U	0339U	0359U	0403U

Other codes (investigational, not medically necessary, etc.):

81229	81599*				
0021U	0228U	0343U	0424U	0433U	0495U

*If the test has no specific code, includes multiple assays, uses an algorithmic analysis and is reported as a numeric score or probability.

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Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

This policy is informed by the most recent National Comprehensive Cancer Network (NCCN) Guidelines® for Prostate Cancer Early Detection version available at the time of the policy review.[6] The information contained in this policy, including specific tests that are listed as included or excluded, is reviewed annually.

Criteria in inclusions are based on the NCCN Guidelines® algorithm footnotes.
Biomarkers that are excluded on this policy are identified by the NCCN Guidelines as investigational or are not discussed.

Table 2. Biomarker Tests Recommended Prior to Initial Biopsy

Biomarker Test	Specimen Source	Testing Targets
Percent-free PSA	Serum	Unbound or free PSA (fPSA), expressed as a ratio of total PSA (tPSA).
PHI	Serum	A combination of the tPSA, fPSA, and proPSA tests. FDA approved.
4Kscore	Serum	A combination of fPSA, tPSA, human kallikrein 2 (hK2) and intact PSA – and also considers age, DRE results, and prior biopsy status.
ExoDx Prostate (Intelliscore) (also, EPI)	Urine	Evaluates a urine-based 3-gene exosome expression assay utilizing *PCA3* and *ERG* (v-ets erythroblastosis virus E26 oncogene homologs) RNA from urine, normalized to SPDEF.
SelectMDx	Urine	Measures *DLX1* and *HOXC6* expression against *KLK3*.
MyProstateScore 2.0 (MPS2)	Urine	Measures expression of *TMPRSS2:ERG, SCHLAP1, OR51E2, APOC1, PCAT14, CAMKK2, PCA3, B3GNT6, NKAIN1, TFF3, SPON2, PCGEM1, TRGV9, PCGEM1, TMSB15A, ERG, KLK4, HOXC6*
IsoPSA	Serum	Measures structural changes (isoforms) in the PSA protein

fPSA: free PSA; tPSA: total PSA; SPDEF: SAM pointed domain-containing ETS transcription factor

Table 3. Biomarker Tests Recommended Prior to Repeat Biopsy

Biomarker Test	Specimen Source	Testing Targets
Percent-free PSA	Serum	Unbound or free PSA (fPSA), expressed as a ratio of total PSA (tPSA).
PHI	Serum	A combination of the tPSA, fPSA, and proPSA tests. FDA approved.
Progensa PCA3	Urine	A noncoding, prostate tissue-specific RNA. FDA approved.
4Kscore	Serum	A combination of fPSA, tPSA, human kallikrein 2 (hK2) and intact PSA – and also considers age, DRE results, and prior biopsy status.
ExoDx Prostate (Intelliscore) (also, EPI)	Urine	Evaluates a urine-based 3-gene exosome expression assay utilizing *PCA3* and *ERG* (v-ets erythroblastosis virus E26 oncogene homologs) RNA from urine, normalized to SPDEF.
ConfirmMDx	Tissue	Assessment of hypermethylation of the promoter regions of *GSTP1, APC* and *RASSF1*.
MyProstateScore2.0 (MPS2)	Urine	Measures expression of *TMPRSS2:ERG, SCHLAP1, OR51E2, APOC1, PCAT14, CAMKK2, PCA3, B3GNT6, NKAIN1, TFF3, SPON2, PCGEM1, TRGV9, PCGEM1, TMSB15A, ERG, KLK4, HOXC6*
IsoPSA	Serum	Measures structural changes (isoforms) in the PSA protein

fPSA: free PSA; tPSA: total PSA; SPDEF: SAM pointed domain-containing ETS transcription factor

Subsection Section Summary: Candidate Gene Panels

Numerous studies have demonstrated the association between single nucleotide variants (SNV) and prostate cancer. Gene panels that evaluate the likelihood of prostate cancer on biopsy are in development.

MyProstateScore 2.0

Review of Evidence

Tosoian et al (2024)[7] evaluated multiple biomarker tests that were assessed in the validation cohort, including PSA, a PSA-based risk calculator (PCPTrc), prostate health index (PHI), derived multiplex 2-ge3ne (dmx2) and 3-gene (dmx3) models, the original 2-gene MyProstatScore test (MPS), and the new locked 18-gene MPS2 models. Under a testing approach with 95% sensitivity for Grade Group (GG) >2 cancer, measures of diagnostic accuracy and clinical consequences of testing were calculated in initial and repeat biopsy populations. GG>3 cancer was secondarily-assessed.

Subsection Summary: MyProstate Score 2.0
Per the Tosoian 2024 study for MyProstate Score 2.0 the new 18 gene cancer test was estimated to have higher diagnostic accuracy for Grade Group>2 cancers relative to existing biomarker tests. This test was estimated to reduce unnecessary biopsies preformed while maintaining highly-sensitive detection of Grade Group prostate >2 cancers. The data support the use of the new PCa biomarker testing in individuals with elevated PSA to reduce the potential harm of PCa screening while maintaining its long-term benefits.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

National Comprehensive Cancer Network
The National Comprehensive Cancer Network (NCCN) guidelines v.2.2024 recommend that individuals with a PSA prostate-specific antigen (PSA) level greater than 3 ng/mL undergo workup for benign disease, repeat PSA, and DRE.[6]

The guidelines recommend as part of the workup for benign disease, consider biomarkers that improve the specificity of screening that includes percent free PSA, with consideration of the Prostate Health Index (PHI), SelectMDx, 4K score, and ExoDx Prostate InteliScore (EPI), MyProstate Score (MPS), and IsoPSA in patients who have not yet had a biopsy. NCCN noted that these tests may be especially useful in individuals with PSA levels between 3 ng/mL and 10 ng/mL. NCCN also noted that it is not yet known how these tests could be applied in optimal combination with magnetic resonance imaging (MRI).

In individuals who had a negative biopsy but are thought to be at higher risk, NCCN recommends to consider biomarkers that improve the specificity of screening (category 2A evidence). Tests that should be considered in the post-biopsy setting include percent free PSA 4Kscore, PHI, PSA Density,PCA3, EPIExoDx Prostate IntelliScore (EPI), MPS2.0, IsoPSA, and ConfirmMDx.

- The list of assays with the potential to permit improved detection of Grade Group ≥2 prostate cancers as an adjuvant to PSA screening is growing rapidly. Below, several of

these assays are discussed. Given the lack of validation of the models/algorithms in additional, independent publications, their unclear behavior in other screened populations, and the lack of clarity regarding the incremental value and cost-effectiveness of these assays, however, the panel cannot recommend their routine use at this time. Those examples include: EpiSwitch® Prostate Screening Test, miR Sentinel™ Prostate Cancer Test,

The National Comprehensive Cancer Network (NCCN) guidelines Prostate Cancer V3.2024[8] no mention of biomarkers in this version of guidelines.

Algorithm Footnote Information:[6,8]
"Percent-free PSA may improve cancer detection. The probability of high-grade cancer (Gleason score ≥ 3+4, Grade Group2 or higher) may be further defined utilizing the Prostate Health Index (PHI), SelectMDx, 4Kscore, ExoDx Prostate Test, MyProstateScore (MPS), and IsoPSA."

"Tests that improve specificity in the post-biopsy setting – including percent-free PSA, 4Kscore, PHI, PCA3, ConfirmMDx, MPS2.0 and IsoPSA – should be considered in Individuals thought to be higher risk despite a negative prostate biopsy."

Biomarkers that are excluded on this policy are identified by the NCCN Guidelines® as investigational or are not discussed.

Government Regulations

National:

There is no national coverage determination on this topic. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Local:

Wisconsin Physicians Service Insurance Corporation
Local Coverage Article: Billing and Coding: MolDX: Progensa® PCA3 Assay Coverage Update (A55202)
Original Article Effective Date: 02/16/2017
Revision Effective Date: 12/30/2021
Retirement Date: 07/02/2022

Progensa® PCA3 Assay, an FDA approved test by Gen-Probe Incorporated, is an mRNA expression assay used alone or in combination with other molecular tests for prostate cancer determination to identify Individuals with increased risk of prostate cancer. PCA3 may help to improve the specificity of prostate cancer detection providing additional information about the risk of prostate cancer over the use of the PSA test alone. Based on the ratio of PCA3 mRNA/PSA mRNA x1000, the PCA3 assay is performed on the first urine collected following an attentive digital rectal examination.

PCA3 testing is covered ONLY when all biopsies in previous encounter(s) are negative and when the patient or physician wants to avoid repeat biopsy (watchful waiting).

When the physician plans to biopsy the prostate, MolDX will consider a PCA3 test as investigational and thus, not a covered Medicare benefit. MolDX considers all other indications for PCA3 not reasonable and necessary.

Medical record documentation must indicate the rationale to perform a PCA3 assay. Providers who report a PCA3 service AND perform a biopsy may be referred for additional action.

NOTE: Effective 10/15/2012, MolDX will deny all laboratory developed tests (LDT) for PCA3 as statutorily excluded services that do not support the required clinical utility for the established Medicare benefit category. Only the unmodified FDA approved test, will be reimbursed.

Wisconsin Physicians Service Insurance Corporation
Local Coverage Determination (LCD): MolDX: ConfirmMDx Epigenetic Molecular Assay (L37005)
Original Effective Date: For services performed on or after 07/17/2017
Revision Effective Date: For services performed on or after 11/26/2020
Retirement Date: 08/20/2022

Indications and Limitations of Coverage
WPS GHA will provide limited coverage for the ConfirmMDx epigenetic assay for prostate cancer (MDxHealth, Irvine, CA) to reduce unnecessary repeat prostate biopsies. WPS GHA recognizes that evidence for clinical utility for CONFIRMMDX in Individuals with previous negative prostate biopsy who are being considered for repeat biopsy is promising with evidence of some clinical utility at the current time. WPS GHA believes the clinical studies planned will generate sufficient additional data to demonstrate the utility of CONFIRMMDX in males with previous negative prostate biopsy who are being considered for repeat biopsy. Continued coverage of CONFIRMMDX for males with previous negative prostate biopsy who are being considered for repeat biopsy will be dependent on semi-annual review of interim data, and/or peer-reviewed publications and/or presentations of clinical utility data demonstrating CONFIRMMDX for males with previous negative prostate biopsy directs patient management as measured using clinical endpoints in one or more studies.

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

Wisconsin Physicians Service Insurance Corporation
Local Coverage Determination (LCD): MolDX: 4KSCORE Assay (L37013)

Original Effective Date: For services performed on or after 07/17/2017
Revision Effective Date: For services performed on or after 09/30/2021
Retirement Date 10/17/2022

Coverage Indications, Limitations, and/or Medical Necessity
This is a non-coverage policy for the 4KSCOREscore® assay (developed by OPKO; marketed by BioReference Laboratory, NJ). This test is a laboratory developed test (LDT) and has not undergone Food and Drug Administration (FDA) review or scrutiny.

Consequently, due to significant issues with assay validation and absence of clinical utility, 4KSCOREscore testing is not reasonable and necessary and is not covered by Medicare.

[For review of the evidence, access the LCD]

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Genetic Testing - Gene Expression Profile Analysis for Risk Stratification for Prostate Cancer Management
- Prostate Specific Antigen Blood Screenings (PSA) - Retired
- Saturation Biopsy for Diagnosis and Staging of Prostate Cancer
- Systems Pathology for Predicting Risk in Prostate Cancer - Retired

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References

1. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2014. Bethesda, MD: National Cancer Institute; 2017
2. Odedina FT, Akinremi TO, Chinegwundoh F, et al. Prostate cancer disparities in Black men of African descent: a comparative literature review of prostate cancer burden among Black men in the United States, Caribbean, United Kingdom, and West Africa. Infect Agent Cancer. Feb 10 2009;4 Suppl 1:S2. PMID 19208207
3. Bell KJ, Del Mar C, Wright G, et al. Prevalence of incidental prostate cancer: A systematic review of autopsy studies. Int J Cancer. Oct 01 2015;137(7):1749-1757. PMID 25821151
4. Gleason DF. Classification of prostatic carcinomas. Cancer Chemother Rep. Mar 1966;50(3):125-128. PMID 5948714
5. National Cancer Institute. SEER Database. 2018; https://seer.cancer.gov/seerinquiry/index.php?page=view&id=20170036&type=q Accessed 2/25/24
6. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: prostate cancer early detection V.2.2024, March 6, 2024 https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf accessed 8/12/24

7. Tosoian, JJ,MD,Alice Yu,Wayne Brisbane The Journal of Urology Feb 2024. Point of View: Innovation and progress for Screening and Management of Localized Prostate Cancer: What an exciting Time Point of View: Innovation and Progress for Screening and Management of Localized Prostate Cancer: What an Exciting Time | Journal of Urology (auajournals.org)
8. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Prostate Cancer 4.2024.May 17, 2024 prostate.pdf prostate.pdf (nccn.org) Accessed 8/12/24
9. Retired: Wisconsin Physicians Service Insurance Corporation. Local Coverage Article: Billing and Coding: MolDX: Progensa® PCA3 Assay Coverage Update (A55202). Original Article Effective Date: 02/16/2017. Revision Effective Date: 12/30/21.
10. Retired: Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): MolDX: ConfirmMDx Epigenetic Molecular Assay (L37005). Original Effective Date: For services performed on or after 07/17/2017. Revision Effective Date: For services performed on or after 11/26/20.
11. Retired: Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): MolDX: 4KSCORE Assay (L37013). Original Effective Date: For services performed on or after 07/17/2017. Revision Effective Date: For services performed on or after 09/30/2021.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 8/12/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
3/1/13	12/11/12	12/31/12	Joint policy established
5/1/14	2/24/14	3/3/14	Routine maintenance Procedure code 88299 removed and replaced with CPT code 81479
9/1/14	6/17/14	6/23/14	Routine maintenance, added MiPS test to policy
7/1/15	4/24/15	5/8/15	Routine maintenance Added procedure code 81313; deleted NOC code Added local Medicare coverage policies
7/1/16	4/19/16	4/19/16	Routine maintenance – Added procedure codes 0010M and 81479. Changed policy title from “Gene-Based Tests for Screening, Detection, and/or Management of Prostate Cancer” to “Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer.” Modified language in medical policy statement. Description, rationale and references updated.
5/1/17	3/8/17	3/16/17	Routine maintenance Added procedure code 81539 and 81599; deleted code 0010M. Updated Government Regulations. Added the following to medical policy statement: “Single-nucleotide polymorphism testing for cancer risk assessment of prostate cancer is considered experimental/ investigational. Added Prostate Health Index (phi) test to policy.
5/1/18	2/20/18	2/20/18	Routine maintenance

			Rationale, Government Regulations and References updated
3/1/19	12/11/18		Routine maintenance Added SelectMDx, ExoDx Prostate IntelliScore, and Apifiny tests Reference to Decipher deleted Added codes: 81551, 88377, 0005U, 0012U
3/1/20	12/17/19		Routine maintenance
3/1/21	12/15/20		Routine maintenance References added: 38, 40, 42, 44, 46, 49
6/15/21			Policy tabled at June 2021 JUMP
7/1/22	4/19/22		Title change from “Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer” to “Prostate Cancer Early Detection: Biomarkers Prior to Biopsy”. Change in position from E/I to covered: MPS, inclusions, exclusions, rationale updated.
7/1/23	4/18/23		Annual Review (jf) Vendor Managed: Avalon 81479 removed Unlisted molecular pathology [eg, SelectMDx®] Added per code Update: 8/5/22: new U code EFD 10/1/22 0339U [eg, SelectMDx®] (EST), 0343U [mirSentinel] E/I not listed in NCCN guidelines. Added NCCN to supplemental information as our reference to biomarkers used in the policy.
9/1/23	6/13/23		Maintenance Code Update (jf) Vendor Managed: NA Added code as EST 0359U remove 81599 code effective 1/1/23 per inquiry from code update. Delete 81599 code when representing IsoPSA.

			Edits to Inclusions added “Prostate cancer early detection” in front of NCCN Guidelines. Edits to Exclusions: Added: (this is not an all-inclusive biomarker list)
7/1/24	4/16/24		Annual Review (jf) Maintenance Code Update Vendor Managed: NA Ref 7,8,9 added 2024 Code Update: Add 0433U and 0424U as E/I effective 1/1/24. Literature Review and email from Lynx Dx o Added code 0403U MyProstateScore 2.0 as EST. Has replaced LynxDX’s original MyProstateScore 0113U o 0113U deleted from policy - Deleted code 88377 from internal section of policy as code was replaced with code 0013U in 2022. Minor Edits to the made to the inclusions and MPS Exclusions added: • Repeat biomarker testing for same indications o EpiSwitch® Prostate Screening Test o miR Sentinel™ Prostate Cancer Test Addition to MPS: Other biomarker genetic testing for prostate cancer that does not meet our inclusionary criteria is considered experimental/investigational. Results of this testing has not been shown to improve clinical health outcomes. Post JUMP: • Edits to the inclusions about the age Add “over” in front of 40 and 45 removal of 75 of age

			• edit under inclusions of language about family history. ○ Edit to the exclusion to Biomarker testing is not expected to be performed more frequently than every 12 months and can only be performed when there is a clinical change. (Ex: significant PSA change)
1/1/25	10/15/24		2024 PLA Code update Minor Edits effective 10/1/24 (jf) Code Update -Add 0495U as E/I Vendor managed: NA Added Stockholm3 as an exclusion - Supplemental Information moved after the rationale section

Next Review Date: 2nd Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PROSTATE CANCER EARLY DETECTION: BIOMARKERS PRIOR TO BIOPSY

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered
BCNA (Medicare Advantage)	See the Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.