

Medical Coverage Policy | Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer



EFFECTIVE DATE: 05 | 01 | 2026

POLICY LAST REVIEWED: 01 | 21 | 2026

OVERVIEW

Various genetic and protein biomarkers are associated with prostate cancer. These tests have the potential to improve the accuracy of differentiating which men should undergo prostate biopsy or rebiopsy after a prior negative biopsy.

The following tests are addressed in this policy:

- Apifyny (Exact Sciences), CPT Code 0021U
- MyProstateScore (MPS) (Lynx Dx), CPT Code 0113U
- PanGIA Prostate (Genetics Institute of America), CPT Code 0228U
- MiCheck® Prostate (Minomic®, Inc.), CPT Code 0591U
- Prostate Health Index (phi) (Beckman Coulter), CPT Code 81479
- Prostate Core Mitomics Test (Mitomics), CPT Code 81479

MEDICAL CRITERIA

Medicare Advantage Plans and Commercial Products

MyProstateScore (MPS), CPT Code 0113U

MPS may be considered medically necessary when the following criteria for numbers 1 through 3 are met:

1. The test is ordered only once per year by a physician or other qualified health care professional (i.e., NP, CNS, PA) AND one of the following:
 - a. Prior to potential biopsy for men \geq 45 years old; OR
 - b. Men who need a repeat biopsy in the setting of individuals thought to be at higher risk despite a prior negative biopsy with confirmed moderately elevated PSA ($>3\text{ng/ml}$ and $<10\text{ng/ml}$; or PSA $>4\text{ng/ml}$ and $<10\text{ng/ml}$ in men >75 years of age)*PSA elevation should be confirmed after a few weeks under standardized conditions (i.e., no ejaculation, manipulations, and urinary tract infections) in the same laboratory before considering a biopsy.
2. AND no other relative indication for prostate biopsy including ANY of the following:
 - a. DRE suspicious for cancer (e.g., nodules, induration, or asymmetry)
 - b. Positive multiparametric MRI (Prostate Imaging Reporting and Data System [PI-RADS] ≥ 3) (if available)
 - c. Positive prior biopsy (cancer Grade Group ≥ 1 , intraductal carcinoma (IDC), atypical intraductal proliferation (AIP))
 - d. Other major risk factor for prostate cancer including:
 - i. Ethnicity at higher risk for prostate cancer
 - ii. First-degree relative with prostate cancer
 - iii. High-penetrance prostate cancer risk gene(s) per NCCN (if known)
3. AND no other relative contraindication for prostate biopsy including ANY of the following:
 - a. <10 year life expectancy, or otherwise not a candidate for prostate cancer treatment
 - b. Invasive treatment for benign prostatic disease or taking medications that influence serum PSA levels within 6 months.
 - c. Active prostatitis on antibiotics

Medicare Advantage Plans and Commercial Products

Unless otherwise noted, for any test filed with an Unlisted CPT code, the medical necessity criteria in the Genetic Testing Services policy would be used. Please see the Related Policies section.

PRIOR AUTHORIZATION

Medicare Advantage Plans and Commercial Products

Prior authorization is required for Medicare Advantage Plans and recommended for Commercial Products and is obtained via the online tool for participating providers for the following test(s):

- MyProstateScore (MPS)

There is no specific CPT coding for some of the services referenced in this policy. Therefore, an Unlisted CPT code should be used (see Coding Section for details). All Unlisted genetic testing CPT codes require prior authorization to determine what service is being rendered and if the service is covered or not medically necessary. See the Related Policies section.

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

POLICY STATEMENT

The following test is covered, but due to the instruction to file an Unlisted CPT code, prior authorization is required:

- Prostate Health Index (phi)

The following test(s) are considered medically necessary when the medical criteria above are met:

- MyProstateScore (MPS)

The following genetic and protein biomarkers for the diagnosis of prostate cancer are considered not covered for Medicare Advantage Plans and not medically necessary for Commercial Products as the evidence is insufficient to determine that the technology results in an improvement in the net health outcome:

- Apifyn
- PanGIA Prostate
- MiCheck®Prostate
- Mitochondrial DNA variant testing (eg, Prostate Core Mitomics Test)
- Candidate gene panels

Single nucleotide variant testing for cancer risk assessment of prostate cancer is not covered as the evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Commercial Products

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. §27-19-81 described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies.

Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate section of the Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for applicable laboratory testing and not medically necessary/not covered benefits/coverage.

BACKGROUND

Prostate cancer is the most common cancer, and the second most common 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 treated 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 patients 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 United States is approximately 16%, while the risk of dying of prostate cancer is 3%. African-American men have the highest prostate cancer risk in the United States; 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. 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, 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. 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.

Numerous genetic alterations associated with development or progression of prostate cancer have been described, with the potential for the use of these molecular markers to improve the selection process of men who should undergo prostate biopsy or rebiopsy after an initial negative biopsy.

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Laboratories that offer laboratory-developed tests must be licensed under the CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration (FDA) has chosen not to require any regulatory review of these tests.

In June 2012, proPSA, a blood test used to calculate the Prostate Health Index (phi; Beckman Coulter) was approved by the FDA through the premarket approval process. The phi test is indicated as an aid to distinguish prostate cancer from a 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.

Biomarkers can help stratify men who have an elevated PSA into those more likely versus less likely to have aggressive disease. These non-invasive biomarker tests have demonstrated that they can (1) reduce the need for unnecessary biopsies in men unlikely to have prostate cancer or high-grade prostate cancer and/or (2) better define men at risk for higher-grade prostate cancer. There is adequate evidence to show that the incremental information provided by validated molecular biomarker tests for prostate cancer in samples of patients whose findings can be generalized to the Medicare population, changes physician management in a way that improves outcomes.

Apify uses an algorithm to score the detection of 8 autoantibodies (ARF 6, NKX3-1, 5' -UTR-BMI1, CEP 164, 3' -UTR-Ropporin, Desmocollin, AURKAIP-1, CSNK2A2) in serum. The identified biomarkers play a role in processes such as androgen response regulation and cellular structural integrity and are proteins that are thought to play a role in prostate tumorigenesis.

MyProstateScore measures TMPRSS2-ERG gene fusion and calculates a probability score that incorporates serum PSA or the PCPT, and urine TMPRSS2-ERG and PCA3 scores.

PanGIA Prostate is a urine test that uses a device with binding pockets for small molecules, proteins, and cells. Results are uploaded to the cloud and a machine learning algorithm compares the results with a signature from patients who have had a positive biopsy and patients who have had a negative prostate biopsy. The report includes a diagnosis with the level of confidence in the diagnosis.

MiCheck® Prostate is an algorithm that combines the testing results of three Abbott ARCHITECT™ serum immunoassays (total prostate specific antigen [tPSA], free PSA [fPSA] and Human Epididymal Protein 4 [HE4]) and one clinical factor (i.e. the patient's Age). The MiCheck Prostate algorithm combines these results to calculate a Percentage Risk Score, which provides an indication of the likelihood of the presence of clinically significant Prostate Cancer (csPCa) (Gleason score >3+4) and is called the MiCheck %Risk of csPCa. Evidence on the MiCheck Prostate test is preliminary. The MiCheck Prostate test showed a sensitivity of 95% and NPV of 92% for aggressive prostate cancer in men over 40 years of age irrespective of PSA levels. The primary limitations of the study were the nonrandomized retrospective study design and the small sample size comprised of an exclusive contemporary U.S. population. No randomized controlled trials (RCTs) were identified using the MiCheck Prostate test. It is unclear from the nonrandomized trial whether the test is intended to be used in addition to repeat PSA and %fPSA, or if the test is intended to be used as a replacement for the current standard of care. The main impact of the test was to decrease the overall number of biopsies without delaying diagnosis for prostate cancer patients.

For individuals who are being considered for an initial prostate biopsy who receive testing for genetic and protein biomarkers of prostate cancer (eg, PanGIA Prostate, Apify), the evidence includes systematic reviews, meta-analyses, and primarily observational studies. Relevant outcomes are overall survival, disease-specific survival, test validity, resource utilization, and quality of life. The evidence supporting clinical utility varies by test. Absent direct evidence of clinical utility, a chain of evidence might be constructed. However, the performance of biomarker testing for directing biopsy referrals is uncertain. While some studies have shown a reduction or delay in biopsy based on testing, a chain of evidence for clinical utility cannot be constructed due to limitations in clinical validity. Test validation populations have included men with a positive digital rectal exam (DRE), a prostate-specific antigen (PSA) level outside of the gray zone (between 3 or 4 ng/mL and 10 ng/mL), or older men for whom the information from test results are less likely to be informative. Many biomarker tests do not have standardized cutoffs to recommend a biopsy. In addition, comparative studies of the many biomarkers are lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are being considered for repeat biopsy who receive testing for genetic and protein biomarkers of prostate cancer (eg, Prostate Core Mitomics Test), the evidence includes systematic reviews and meta-analyses and primarily observational studies. Relevant outcomes are overall survival, disease-specific survival, test validity, resource utilization, and quality of life. The performance of biomarker testing for guiding rebiopsy decisions is lacking. The tests are associated with a diagnosis of prostate cancer and aggressive prostate cancer, but studies on clinical validity are limited and do not compare performance characteristics with standard risk prediction models. Direct evidence supporting clinical utility has not been shown. No data are currently available on physician decisions on rebiopsy or on the longer-term clinical outcomes of men who did not have a biopsy based on test results. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CODING

Medicare Advantage Plans and Commercial Products

The following CPT code(s) are considered medically necessary when the medical criteria above are met.

This code can be used for MyProstateScore (MPS):

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

The following CPT code(s) are not covered for Medicare Advantage Plans and are not medically necessary for Commercial Products.

This code can be used for Apifyny:

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

This code can be used for PanGIA Prostate:

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

This code can be used for MiCheck®Prostate:

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 (New Code Effective 10/1/2025)

The following Unlisted CPT code requires prior authorization. The code can be used for any test identified in this policy that does not have a specific CPT code, including Prostate Health Index (phi).

81479 Unlisted molecular pathology procedure

RELATED POLICIES

Biomarker Testing Mandate

Genetic Testing Services

Medical Necessity

Proprietary Laboratory Analyses (PLA) and Multianalyte Assays with Algorithmic Analyses (MAAA)

Serum Tumor Markers for Breast and Gastrointestinal Malignancies

Unlisted Procedures

Urinary Biomarkers for Cancer Screening, Diagnosis and Surveillance

PUBLISHED

Provider Update, March 2026

Provider Update, January/July/November 2025

Provider Update, February/June/August/November 2023

Provider Update, March 2022

Provider Update, May 2020

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD): Prostate Specific Antigen (190.31)
2. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Billing and Coding: Biomarker Testing (Prior to Initial Biopsy) for Prostate Cancer Diagnosis (A56609)
3. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): MolDX: Molecular Diagnostic Tests (MDT) (L36807)
4. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT) (A57772)

5. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD): L35062 - Biomarkers Overview (L35602)
6. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article: Billing and Coding: Molecular Pathology and Genetic Testing (A58917)
7. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2014. Bethesda, MD: National Cancer Institute; 2017.
8. 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
9. 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): 1749-57. PMID 25821151
10. Gleason DF. Classification of prostatic carcinomas. *Cancer Chemother Rep*. Mar 1966; 50(3): 125-8. PMID 5948714
11. National Cancer Institute. SEER Database. <https://seer.cancer.gov/seerinqury/index.php?page=view&id=20170036&type=q>. Accessed September 25, 2025.
12. Hoogendam A, Buntinx F, de Vet HC. The diagnostic value of digital rectal examination in primary care screening for prostate cancer: a meta-analysis. *Fam Pract*. Dec 1999; 16(6): 621-6. PMID 10625141
13. Gosselaar C, Roobol MJ, Roemeling S, et al. The role of the digital rectal examination in subsequent screening visits in the European randomized study of screening for prostate cancer (ERSPC), Rotterdam. *Eur Urol*. Sep 2008; 54(3): 581-8. PMID 18423977
14. Thompson IM, Pauler DK, Goodman PJ, et al. Prevalence of prostate cancer among men with a prostate-specific antigen level or =4.0 ng per milliliter. *N Engl J Med*. May 27 2004; 350(22): 2239-46. PMID 15163773
15. Catalona WJ, Smith DS, Ratliff TL, et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. *N Engl J Med*. Apr 25 1991; 324(17): 1156-61. PMID 1707140
16. Aus G, Bergdahl S, Lodding P, et al. Prostate cancer screening decreases the absolute risk of being diagnosed with advanced prostate cancer--results from a prospective, population-based randomized controlled trial. *Eur Urol*. Mar 2007; 51(3): 659-64. PMID 16934392
17. Buzzoni C, Auvinen A, Roobol MJ, et al. Metastatic Prostate Cancer Incidence and Prostate-specific Antigen Testing: New Insights from the European Randomized Study of Screening for Prostate Cancer. *Eur Urol*. Nov 2015; 68(5): 885-90. PMID 25791513
18. Arnsrud Godtman R, Holmberg E, Lilja H, et al. Opportunistic testing versus organized prostate-specific antigen screening: outcome after 18 years in the Goteborg randomized population-based prostate cancer screening trial. *Eur Urol*. Sep 2015; 68(3): 354-60. PMID 25556937
19. Hugosson J, Carlsson S, Aus G, et al. Mortality results from the Goteborg randomised population-based prostate-cancer screening trial. *Lancet Oncol*. Aug 2010; 11(8): 725-32. PMID 20598634
20. Schroder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med*. Mar 26 2009; 360(13): 1320-8. PMID 19297566
21. Wolf AM, Wender RC, Etzioni RB, et al. American Cancer Society guideline for the early detection of prostate cancer: update 2010. *CA Cancer J Clin*. Mar-Apr 2010; 60(2): 70-98. PMID 20200110
22. Rosario DJ, Lane JA, Metcalfe C, et al. Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study. *BMJ*. Jan 09 2012; 344: d7894. PMID 22232535
23. Lavallee LT, Binette A, Witiuk K, et al. Reducing the Harm of Prostate Cancer Screening: Repeated Prostate-Specific Antigen Testing. *Mayo Clin Proc*. Jan 2016; 91(1): 17-22. PMID 26688045
24. Ruiz-Aragon J, Marquez-Pelaez S. [Assessment of the PCA3 test for prostate cancer diagnosis: a systematic review and meta-analysis]. *Actas Urol Esp*. Apr 2010; 34(4): 346-55. PMID 20470697
25. Mackinnon AC, Yan BC, Joseph LJ, et al. Molecular biology underlying the clinical heterogeneity of prostate cancer: an update. *Arch Pathol Lab Med*. Jul 2009; 133(7): 1033-40. PMID 19642730
26. Partin AW, Brawer MK, Subong EN, et al. Prospective evaluation of percent free-PSA and complexed-PSA for early detection of prostate cancer. *Prostate Cancer Prostatic Dis*. Jun 1998; 1(4): 197-203. PMID 12496895

27. Thompson IM, Ankerst DP, Chi C, et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. *J Natl Cancer Inst.* Apr 19 2006; 98(8): 529-34. PMID 16622122
28. van Vugt HA, Roobol MJ, Kranse R, et al. Prediction of prostate cancer in unscreened men: external validation of a risk calculator. *Eur J Cancer.* Apr 2011; 47(6): 903-9. PMID 21163642
29. Rosenkrantz AB, Verma S, Choyke P, et al. Prostate Magnetic Resonance Imaging and Magnetic Resonance Imaging Targeted Biopsy in Patients with a Prior Negative Biopsy: A Consensus Statement by AUA and SAR. *J Urol.* Dec 2016; 196(6): 1613-1618. PMID 27320841
30. Kawada T, Shim SR, Quhal F, et al. Diagnostic Accuracy of Liquid Biomarkers for Clinically Significant Prostate Cancer Detection: A Systematic Review and Diagnostic Meta-analysis of Multiple Thresholds. *Eur Urol Oncol.* Aug 2024; 7(4): 649-662. PMID 37981495
31. Russo GI, Regis F, Castelli T, et al. A Systematic Review and Meta-analysis of the Diagnostic Accuracy of Prostate Health Index and 4-Kallikrein Panel Score in Predicting Overall and High-grade Prostate Cancer. *Clin Genitourin Cancer.* Aug 2017; 15(4): 429-439.e1. PMID 28111174
32. Stattin P, Vickers AJ, Sjoberg DD, et al. Improving the Specificity of Screening for Lethal Prostate Cancer Using Prostate-specific Antigen and a Panel of Kallikrein Markers: A Nested Case-Control Study. *Eur Urol.* Aug 2015; 68(2): 207-13. PMID 25682340
33. Loeb S, Shin SS, Broyles DL, et al. Prostate Health Index improves multivariable risk prediction of aggressive prostate cancer. *BJU Int.* Jul 2017; 120(1): 61-68. PMID 27743489
34. Pecoraro V, Roli L, Plebani M, et al. Clinical utility of the (-2)proPSA and evaluation of the evidence: a systematic review. *Clin Chem Lab Med.* Jul 01 2016; 54(7): 1123-32. PMID 26609863
35. Anyango R, Ojwando J, Mwita C, et al. Diagnostic accuracy of [-2]proPSA versus Gleason score and Prostate Health Index versus Gleason score for the determination of aggressive prostate cancer: a systematic review. *JBI Evid Synth.* Mar 17 2021; 19(6): 1263-1291. PMID 33741840
36. Catalona WJ, Partin AW, Sanda MG, et al. A multicenter study of [-2]pro-prostate specific antigen combined with prostate specific antigen and free prostate specific antigen for prostate cancer detection in the 2.0 to 10.0 ng/ml prostate specific antigen range. *J Urol.* May 2011; 185(5): 1650-5. PMID 21419439
37. Tosoian JJ, Druskin SC, Andreas D, et al. Use of the Prostate Health Index for detection of prostate cancer: results from a large academic practice. *Prostate Cancer Prostatic Dis.* Jun 2017; 20(2): 228-233. PMID 28117387
38. White J, Shenoy BV, Tutrone RF, et al. Clinical utility of the Prostate Health Index (phi) for biopsy decision management in a large group urology practice setting. *Prostate Cancer Prostatic Dis.* Apr 2018; 21(1): 78-84. PMID 29158509
39. Sanda MG, Feng Z, Howard DH, et al. Association Between Combined TMPRSS2:ERG and PCA3 RNA Urinary Testing and Detection of Aggressive Prostate Cancer. *JAMA Oncol.* Aug 01 2017; 3(8): 1085-1093. PMID 28520829
40. Tomlins SA, Day JR, Lonigro RJ, et al. Urine TMPRSS2:ERG Plus PCA3 for Individualized Prostate Cancer Risk Assessment. *Eur Urol.* Jul 2016; 70(1): 45-53. PMID 25985884
41. Ankerst DP, Goros M, Tomlins SA, et al. Incorporation of Urinary Prostate Cancer Antigen 3 and TMPRSS2:ERG into Prostate Cancer Prevention Trial Risk Calculator. *Eur Urol Focus.* Jan 2019; 5(1): 54-61. PMID 29422418
42. Tosoian JJ, Trock BJ, Morgan TM, et al. Use of the MyProstateScore Test to Rule Out Clinically Significant Cancer: Validation of a Straightforward Clinical Testing Approach. *J Urol.* Mar 2021; 205(3): 732-739. PMID 33080150
43. Newcomb LF, Zheng Y, Faino AV, et al. Performance of PCA3 and TMPRSS2:ERG urinary biomarkers in prediction of biopsy outcome in the Canary Prostate Active Surveillance Study (PASS). *Prostate Cancer Prostatic Dis.* Sep 2019; 22(3): 438-445. PMID 30664734
44. Van Neste L, Hendriks RJ, Dijkstra S, et al. Detection of High-grade Prostate Cancer Using a Urinary Molecular Biomarker-Based Risk Score. *Eur Urol.* Nov 2016; 70(5): 740-748. PMID 27108162
45. McKiernan J, Donovan MJ, O'Neill V, et al. A Novel Urine Exosome Gene Expression Assay to Predict High-grade Prostate Cancer at Initial Biopsy. *JAMA Oncol.* Jul 01 2016; 2(7): 882-9. PMID 27032035
46. Schipper M, Wang G, Giles N, et al. Novel prostate cancer biomarkers derived from autoantibody signatures. *Transl Oncol.* Apr 2015; 8(2): 106-11. PMID 25926076
47. Shore ND, Piczonka CM, Henderson RJ, et al. Development and evaluation of the MiCheck test for aggressive prostate cancer. *Urol Oncol.* Aug 2020; 38(8): 683.e11-683.e18. PMID 32305266

48. Gillatt D, Polikarpov D, Smith I, Lau H, Kim L, Huynh CC, et al. MP17-07VALIDATION OF MICHECKPROSTATE FOR SIGNIFICANT PROSTATE CANCER IN AN AUSTRALIAN POPULATION. *Journal of Urology* [Internet]. 2023 Apr 1; 209(Supplement 4):e215.
49. Cui Y, Cao W, Li Q, et al. Evaluation of prostate cancer antigen 3 for detecting prostate cancer: a systematic review and meta-analysis. *Sci Rep*. May 10 2016; 6: 25776. PMID 27161545
50. Rodriguez SVM, Garcia-Perdomo HA. Diagnostic accuracy of prostate cancer antigen 3 (PCA3) prior to first prostate biopsy: A systematic review and meta-analysis. *Can Urol Assoc J*. May 2020; 14(5): E214-E219. PMID 31793864
51. Wei JT, Feng Z, Partin AW, et al. Can urinary PCA3 supplement PSA in the early detection of prostate cancer?. *J Clin Oncol*. Dec 20 2014; 32(36): 4066-72. PMID 25385735
52. Hennenlotter J, Neumann T, Alperowitz S, et al. Age-Adapted Prostate Cancer Gene 3 Score Interpretation - Suggestions for Clinical Use. *Clin Lab*. Mar 01 2020; 66(3). PMID 32162868
53. Vickers AJ, Gupta A, Savage CJ, et al. A panel of kallikrein marker predicts prostate cancer in a large, population-based cohort followed for 15 years without screening. *Cancer Epidemiol Biomarkers Prev*. Feb 2011; 20(2): 255-61. PMID 21148123
54. Ruffion A, Devonec M, Champetier D, et al. PCA3 and PCA3-based nomograms improve diagnostic accuracy in patients undergoing first prostate biopsy. *Int J Mol Sci*. Aug 29 2013; 14(9): 17767-80. PMID 23994838
55. Ruffion A, Perrin P, Devonec M, et al. Additional value of PCA3 density to predict initial prostate biopsy outcome. *World J Urol*. Aug 2014; 32(4): 917-23. PMID 24500192
56. Merdan S, Tomlins SA, Barnett CL, et al. Assessment of long-term outcomes associated with urinary prostate cancer antigen 3 and TMPRSS2:ERG gene fusion at repeat biopsy. *Cancer*. Nov 15 2015; 121(22): 4071-9. PMID 26280815
57. Djavan B, Waldert M, Zlotta A, et al. Safety and morbidity of first and repeat transrectal ultrasound guided prostate needle biopsies: results of a prospective European prostate cancer detection study. *J Urol*. Sep 2001; 166(3): 856-60. PMID 11490233
58. Lujan M, Paez A, Santonja C, et al. Prostate cancer detection and tumor characteristics in men with multiple biopsy sessions. *Prostate Cancer Prostatic Dis*. 2004; 7(3): 238-42. PMID 15289810
59. Stewart GD, Van Neste L, Delvenne P, et al. Clinical utility of an epigenetic assay to detect occult prostate cancer in histopathologically negative biopsies: results of the MATLOC study. *J Urol*. Mar 2013; 189(3): 1110-6. PMID 22999998
60. Partin AW, Van Neste L, Klein EA, et al. Clinical validation of an epigenetic assay to predict negative histopathological results in repeat prostate biopsies. *J Urol*. Oct 2014; 192(4): 1081-7. PMID 24747657
61. Waterhouse RL, Van Neste L, Moses KA, et al. Evaluation of an Epigenetic Assay for Predicting Repeat Prostate Biopsy Outcome in African American Men. *Urology*. Jun 2019; 128: 62-65. PMID 29660369
62. Van Neste L, Partin AW, Stewart GD, et al. Risk score predicts high-grade prostate cancer in DNA-methylation positive, histopathologically negative biopsies. *Prostate*. Sep 2016; 76(12): 1078-87. PMID 27121847
63. Partin AW, VAN Crieking W, Trock BJ, et al. CLINICAL EVALUATION OF AN EPIGENETIC ASSAY TO PREDICT MISSED CANCER IN PROSTATE BIOPSY SPECIMENS. *Trans Am Clin Climatol Assoc*. 2016; 127: 313-327. PMID 28066067
64. Food and Drug Administration. Summary of Safety and Effectiveness Data. PMA P090026. Quantitative test for determination of [-2]proPSA levels. Silver Spring, MD: Food and Drug Administration; 2012.
65. Aubry W, Lieberthal R, Willis A, et al. Budget impact model: epigenetic assay can help avoid unnecessary repeated prostate biopsies and reduce healthcare spending. *Am Health Drug Benefits*. Jan 2013; 6(1): 15-24. PMID 24991343
66. Robinson K, Creed J, Reguly B, et al. Accurate prediction of repeat prostate biopsy outcomes by a mitochondrial DNA deletion assay. *Prostate Cancer Prostatic Dis*. Jun 2010; 13(2): 126-31. PMID 20084081
67. Legisi L, DeSa E, Qureshi MN. Use of the Prostate Core Mitomic Test in Repeated Biopsy Decision-Making: Real-World Assessment of Clinical Utility in a Multicenter Patient Population. *Am Health Drug Benefits*. Dec 2016; 9(9): 497-502. PMID 28465777
68. Leyten GH, Hessels D, Smit FP, et al. Identification of a Candidate Gene Panel for the Early Diagnosis of Prostate Cancer. *Clin Cancer Res*. Jul 01 2015; 21(13): 3061-70. PMID 25788493

69. Xiao K, Guo J, Zhang X, et al. Use of two gene panels for prostate cancer diagnosis and patient risk stratification. *Tumour Biol.* Aug 2016; 37(8): 10115-22. PMID 26820133
70. Tosoian JJ, Sessine MS, Trock BJ, et al. MyProstateScore in men considering repeat biopsy: validation of a simple testing approach. *Prostate Cancer Prostatic Dis.* Sep 2023; 26(3): 563-567. PMID 36585434
71. Wei JT, Barocas D, Carlsson S, et al. Early Detection of Prostate Cancer: AUA/SUO Guideline Part I: Prostate Cancer Screening. *J Urol.* Jul 2023; 210(1): 46-53. PMID 37096582
72. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: prostate cancer early detection.
http://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for NCCN clinical practice guidelines in oncology: prostate cancer early detection V.2.2021 National Comprehensive Cancer Network rights reserved. Accessed September 25, 2025.
73. National Institute for Health and Care Excellence (NICE). Prostate cancer: diagnosis and management [NG131]. 2019; <https://www.nice.org.uk/guidance/ng131/chapter/Recommendations#assessment-and-diagnosis>. Accessed September 25, 2025.
74. U. S. Preventive Services Task Force. Prostate Cancer: Screening. 2018; <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening1>. Accessed September 25, 2025.

CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS

This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member's subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.

