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:

- Apifiny (Exact Sciences), CPT Code 0021U
- MyProstateScore (MPS) (Lynx Dx), CPT Code 0113U
- PanGIA Prostate (Genetics Institute of America), CPT Code 0228U
- MiCheck® Prostate (SoftCell Laboratories LLC), CPT Code 0591U (Laboratory Revised Effective 10/1/2026)
- 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 >/ 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 (>3ng/ml and <10ng/ml; or PSA >/4ng/ml and < 10ng/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:

- Apifiny
- 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.

Apifiny 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 urineTMPRSS2-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 inmen 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, Apifiny), 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 (between3 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 Apifiny:

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), serum, prognostic algorithm incorporating 3 proteins and digital rectal examination, results reported as a probability score for clinically significant prostate cancer (Text Revised Effective 10/1/2026)

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

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