MEDICAL POLICY

POLICY TITLE	GENETIC AND PROTEIN BIOMARKERS FOR THE MANAGEMENT, DIAGNOSIS, AND CANCER RISK ASSESSMENT OF PROSTATE CANCER
POLICY NUMBER	MP-2.280

Effective Date:	1/1/2024

POLICY

Gene expression profile analysis and protein biomarkers to guide the management of prostate cancer may be considered **medically necessary** if the following are met:

Decipher®, for the following indications:

- Post biopsy in members with NCCN low-risk, favorable intermediate-risk, unfavorable intermediate-risk, and high-risk prostate cancer who have a greater than 10-year life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy; or
- Post biopsy in members with intermediate-risk prostate cancer when deciding whether to add androgen-deprivation therapy to radiation; or
- Post-radical prostatectomy to determine adjuvant versus salvage radiation therapy or to determine whether to initiate systemic therapies for either of the following:
    - Rising prostate-specific antigen (PSA) (above nadir); or
    - Undetectable PSA with adverse pathological features. This includes pT2 with positive margins and any pT3 disease (see policy guidelines)

Oncotype DX® Prostate for the following indications post biopsy:

- Members with NCCN low-risk and favorable intermediate-risk prostate cancer who have greater than 10-year life expectancy and who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy; or
- Members with intermediate-risk prostate cancer when deciding whether to add androgen-deprivation therapy to radiation.

Prolaris®, for the following indications post-biopsy:

- Members with NCCN low-risk, favorable intermediate-risk, unfavorable intermediate-risk, and high-risk prostate cancer who have greater than 10-year life expectancy and who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy; *or*
  Members with intermediate-risk prostate cancer when deciding whether to add androgen-deprivation therapy to radiation.

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All other uses of gene expression profile analysis and protein biomarkers to guide the management of prostate cancer is considered **not medically necessary.** There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

The following genetic and protein biomarkers for the diagnosis of prostate cancer are considered **investigational**:

- Kallikrein markers (e.g., 4Kscore™ Test)
- Prostate Health Index (phi)
- HOXC6 and DLX1 testing (e.g., SelectMDx)
- PCA3, ERG, and SPDEF RNA expression in exosomes (e.g., ExoDx Prostate IntelliScore)
- Autoantibodies ARF 6, NKX3-1, 5-UTR-BMI1, CEP 164, 3-UTR-Ropporin, Desmocollin, AURKAIP-1, and CSNK2A2 (e.g., Apifiny)
- PCA3 testing (e.g., Progensa PCA3 Assay)
- *TMPRSS: ERG* fusion genes (e.g., MyProstate Score)
- Gene hypermethylation testing (e.g., ConfirmMDx®)
- Mitochondrial DNA mutation testing (e.g., Prostate Core Mitomics Test™)
- PanGIA Prostate
- miR Sentinel™ Prostate Cancer Test
- Candidate gene panels

Single nucleotide variant testing for cancer risk assessment of prostate cancer is considered **investigational**. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with the above procedures.

The National Comprehensive Cancer Network (NCCN) is a nonprofit alliance of cancer centers throughout the United States. NCCN develops the Clinical Practice Guidelines in Oncology which are recommendations aimed to help health care professionals diagnose, treat, and manage patients with cancer. Guidelines evolve continuously as new treatments and diagnostics emerge and may be used by Capital Blue Cross when determining medical necessity according to this policy.

Policy Guidelines

pT2 is defined as cancer that is confined to the prostate
pT3 is defined as cancer that has grown outside the prostate (extraprostatic extension)

Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being

implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the HUman Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Diseased-Assoc.Variant	Disease-associated change in the DNA sequence.
	Variant	Change in DNA sequence
	Familial Variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives.

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely Pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

American College of Medical Genetics and Genomics; AMP: Association of Molecular Pathology.

Genetic Counseling

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

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Cross-References

MP 2.267 Circulating Tumor DNA and Circulating Tumor Cells for Cancer Management (Liquid Biopsy)

I. PRODUCT VARIATIONS TOP

This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO: Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

II. DESCRIPTION/BACKGROUND TOP

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

Single nucleotide variants (SNVs) occur when a single nucleotide is replaced with another, and are the most common type of genetic variation in humans. They occur normally throughout the genome and can act as biologic markers for disease association. Genome-wide association studies have identified correlations between prostate cancer risk and specific SNVs. However, it is widely accepted that, individually, SNV-associated disease risk is low and of no value in screening, although multiple SNVs in combination may account for a higher proportion of prostate cancer. Investigators have begun to explore the use of algorithms incorporating information from multiple SNVs to increase the clinical value of testing**.**

Gene expression profile analysis and protein biomarkers have been proposed as a means to risk-stratify patients with prostate cancer to guide treatment decisions. These tests are intended to be used either on prostate needle biopsy tissue to guide management decisions for active surveillance or therapeutic intervention, to guide radiotherapy use after radical prostatectomy (RP), or to guide medication selection after progression in metastatic castration-resistant prostate cancer.

PROSTATE CANCER

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 that are unlikely to be life-threatening to aggressive tumors which can metastasize, lead to morbidity or death. Early disease that is localized 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 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%, but 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 ages 55 and 60% of men ages eighty 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.

Localized prostate cancers may appear very similar clinically at diagnosis. However, they often exhibit diverse risk of progression that may not be captured by clinical risk categories (e.g., D'Amico criteria) or prognostic tools based on clinical findings, including PSA titers, Gleason grade, or tumor stage. In studies of conservative management, the risk of localized disease progression based on prostate cancer-specific survival rates at 10 years may range from 15% to 20% to perhaps 27% at 20-year follow-up. Among older men (ages 70 years) with low-risk disease, comorbidities typically supervene as a cause of death; these men will die with prostate cancer present, rather than from cancer itself. Other very similar appearing low-risk tumors may progress unexpectedly rapidly, quickly disseminating and becoming incurable.

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; seven 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 the 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.

Risk Stratification in Newly Diagnosed Disease

In the U. S., most prostate cancers are clinically localized at diagnosis due in part to the widespread use of PSA testing. Clinicopathologic characteristics are used to stratify patients by risk based on the extent of the primary tumor (T category), nearby lymph node involvement (N category), metastasis (M category), PSA level, and Gleason score. The National Comprehensive Cancer Network and American Urological Association risk categories for clinically localized prostate cancer are similar, derived from the D'Amico criteria and broadly include low-, intermediate-, or high-risk as follows as well as subcategories within these groups:

- Low: T1-T2a and Gleason score ≤6/Gleason grade group 1 and PSA level ≤10 ng/mL;
- Intermediate: T2b-T2c or Gleason score 3+4=7/Gleason grade group 2 or Gleason score 4+3=7/Gleason grade group 3 or PSA level 10-20 ng/mL;
- High: T3a or Gleason score 8/Gleason grade group 4 or Gleason score 9-10/Gleason grade group 5 or PSA level >20 ng/mL.

Risk stratification is combined with patient age, life expectancy, and treatment preferences to make initial therapy decisions.

Monitoring After Prostatectomy

All normal prostate tissue and tumor tissue are theoretically removed during radical prostatectomy (RP), so the serum level of PSA should be undetectable following RP. Detectable PSA post-RP indicates residual prostate tissue and presumably persistent or recurrent disease. PSA is serially measured following RP to detect early disease recurrence. The National Comprehensive Cancer Network recommends monitoring serum PSA every 6 to 12 months for the first 5 years and annually thereafter. Many recurrences following RP can be successfully treated. The American Urological Association has recommended that biochemical recurrence be defined as a serum PSA of 0.2 ng/mL or higher, which is confirmed by the second determination with a PSA level of 0.2 ng/mL or higher.

Castration-Resistant Prostate Cancer

Androgen deprivation therapy (ADT) is generally the initial treatment for patients with advanced prostate cancer. ADT can produce tumor response and improve quality of life, but most patients will eventually progress on ADT. Disease that progresses while the patient is on ADT is referred to as castration-resistant prostate cancer. After progression, continued ADT is generally used in conjunction with other treatments. Androgen pathways are important in the progression of castration-resistant prostate cancer. Several drugs have been developed that either inhibit enzymes involved in androgen production or inhibit the androgen receptor, such as abiraterone and enzalutamide. Taxane chemotherapy with docetaxel or cabazitaxel may also be used after progression. Immunotherapy (sipuleucel-T) or radium 223 are options for select men.

REGULATORY STATUS

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. Laboratories that offer laboratory-developed tests must be licensed under the Clinical Laboratory Improvement Amendments for high-complexity testing. Prolaris® (Myriad Genetics), Oncotype DX® Prostate and Oncotype DX AR-V7 Nuclear Detect (Genomic Health), Decipher gene expression profiling test (Decipher Corp), and the ProMark™ protein biomarker test (Metamark Genetics) are available under the auspices of the CLIA. To date, the U.S. Food and Drug Administration (FDA) has chosen not to require any regulatory review of these tests.

In November 2015, the FDA's Office of Public Health Strategy and Analysis published a report suggesting FDA oversight of laboratory-developed tests. The FDA argued that many tests need more FDA oversight than the regulatory requirements of the CLIA. The CLIA standards relate to laboratory operations but do not address inaccuracies or unreliability of specific tests. Prolaris is among the twenty case studies in the document cited as needing FDA oversight. The report asserted that patients are potentially receiving inappropriate prostate cancer care because there is no evidence that results from the test meaningfully improve clinical outcomes

The following laboratories are certified under the Clinical Laboratory Improvement Amendments: BioReference Laboratories and GenPath Diagnostics (subsidiaries of OPKO Health; 4Kscore®), ARUP Laboratories, Mayo Medical Laboratories, LabCorp, BioVantra, others (PCA3 assay), Clinical Research Laboratory (Prostate Core Mitomic Test™), MDx Health (SelectMDx, ConfirMDx), 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) was approved by the FDA through the premarket approval process. The Progensa PCA3 Assay has been approved by the 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) 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 fifty 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.

III. RATIONALE

TOP

Summary of Evidence

For individuals who are being considered for an initial prostate biopsy who receive testing for genetic and protein biomarkers of prostate cancer (e.g., kallikreins biomarkers and 4Kscore Test, proPSA and Prostate Health Index, TMPRSS fusion genes and MyProstate Score, SelectMDx for Prostate Cancer, ExoDx Prostate, Apifiny, PCA3 score, PanGIA Prostate, and miR Sentinel), 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 but has not been directly shown for any biomarker 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, a 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 the effects of the technology on health outcomes.

For individuals who are being considered for repeat biopsy who receive testing for genetic and protein biomarkers of prostate cancer (e.g., PCA3 score, Gene Hypermethylation and ConfirmMDx test, 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 did 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 biopsy based on test results. The evidence is insufficient to determine the effects of the technology on health outcomes.

Initial Management Decision: Active Surveillance versus Therapeutic Intervention

For individuals who have clinically localized untreated prostate cancer who receive Prolaris, the evidence includes retrospective cohort studies of clinical validity using archived samples in patients of mixed risk categories. Relevant outcomes include overall survival (OS), disease-specific survival, quality of life (QOL), and treatment-related morbidity. For the low-risk group, the Prostate Testing for Cancer and Treatment trial showed 99% 10-year disease-specific survival in mostly low-risk patients receiving active surveillance. The low mortality rate estimated with tight precision makes it unlikely that a test intended to identify a subgroup of low-risk men with a net benefit from immediate treatment instead of active surveillance would find such a group. For the intermediate-risk group, the evidence of improved clinical validity or prognostic accuracy for prostate cancer death using Prolaris Cell Cycle Progression score in patients managed conservatively after a needle biopsy has shown some improvement in areas under the receiver operating characteristic curve over clinicopathologic risk stratification tools. There is limited indirect evidence for potential clinical utility. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Input from the NCCN Biomarkers Compendium gives a 2A recommendation for consideration of Prolaris. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have clinically localized untreated prostate cancer who receive Oncotype DX Prostate, the evidence includes case-cohort and retrospective cohort studies of clinical validity using archived samples in patients of mixed risk categories, and a decision-curve analysis examining indirect evidence of clinical utility. Relevant outcomes include OS, disease-specific survival, QOL, and treatment-related morbidity. Evidence for clinical validity and potential clinical utility of Oncotype DX Prostate in patients with clinically localized prostate cancer derives from a study predicting adverse pathology after RP. The validity of using tumor pathology as a surrogate for the risk of progression and cancer-specific death is unclear. It is also unclear whether results from an RP population can be generalized to an active surveillance

population. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Input from the NCCN Biomarkers Compendium gives a 2A recommendation for consideration of Oncotype Dx Prostate. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have clinically localized untreated prostate cancer who receive Decipher Biopsy, the evidence includes retrospective cohort studies of clinical validity using archived samples in intermediate- and high-risk patients and no studies of clinical utility. Relevant outcomes include OS, disease-specific survival, QOL, and treatment-related morbidity. A test designed to identify intermediate-risk men who can receive active surveillance instead of RP or radiotherapy (RT) or high-risk men who can forego androgen deprivation therapy would need to show very high negative predictive value for disease-specific mortality at 10 years and improvement in prediction compared with existing tools used to select such men. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Input from the NCCN Biomarkers Compendium gives a 2A recommendation for consideration of Decipher test. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have clinically localized untreated prostate cancer who receive the ProMark protein biomarker test, the evidence includes a retrospective cohort study of clinical validity using archived samples and no studies of clinical utility. Relevant outcomes include OS, disease-specific survival, QOL, and treatment-related morbidity. Current evidence does not support improved outcomes with ProMark given that only a single clinical validity study is available. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Management Decision After Radical Prostatectomy

For individuals who have localized prostate cancer treated with RP who receive Prolaris, the evidence includes retrospective cohort studies of clinical validity using archived samples. Relevant outcomes include OS, disease-specific survival, QOL, and treatment-related morbidity. No direct evidence is available to support the clinical utility of Prolaris for improving net outcomes of patients with localized prostate cancer following RP. The chain of evidence is also incomplete. Decision-curve analysis did not provide convincing evidence of meaningful improvement in net benefit by incorporating the cell cycle progression (CCP) score. Evidence of improved clinical validity or prognostic accuracy for prostate cancer death using the Prolaris Cell Cycle Progression score in patients after prostatectomy has shown some improvement in areas under the receiver operating characteristic curve over clinicopathologic risk stratification tools. Although Prolaris CCP score may have an association with biochemical recurrence (BCR), disease-specific survival outcomes were reported in only one analysis. A larger number of

disease-specific survival events and precision estimates for discrimination measures are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have localized prostate cancer who are treated with RP and who receive the Decipher RP prostate cancer classifier, the evidence includes a study of analytic validity, prospective and retrospective studies of clinical validity using overlapping archived samples, decision-curve analyses examining indirect evidence of clinical utility, and prospective decision-impact studies without pathology or clinical outcomes. Relevant outcomes include OS, disease-specific survival, QOL, and treatment-related morbidity. The clinical validity of the Decipher RP genomic classifier has been evaluated in samples of patients with high-risk prostate cancer undergoing different interventions following RP. Studies reported some incremental improvement in discrimination. However, it is unclear whether there is consistently improved reclassification-particularly to higher risk categories-or whether the test could be used to predict which men will benefit from radiotherapy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Input from the NCCN Guidelines on Prostate Cancer gives a 2A recommendation for the Decipher test. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Management Decision in Castration-Resistant Prostate Cancer

For individuals who have metastatic castration-resistant prostate cancer who receive the Oncotype DX AR-V7 Nuclear Detect, the evidence includes one prospective cohort study, one retrospective cohort study of clinical validity using archived samples, and no studies of clinical utility. Relevant outcomes include OS, disease-specific survival, QOL, and treatment-related morbidity. Current evidence does not support improved outcomes with Oncotype DX AR-V7 Nuclear Detect, given that only two clinical validity studies meeting inclusion criteria were available. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

IV. DEFINITIONS TOP

NA

V. BENEFIT VARIATIONS TOP

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member’s health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and

providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VI. DISCLAIMER

TOP

Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice, and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VII. CODING INFORMATION

TOP

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Not medically necessary for the management of prostate cancer, therefore not covered:

CPT Codes®								
81479								

Investigational for the diagnosis and cancer risk assessment of prostate cancer, therefore, not covered:

CPT Codes®								
81313	81479	81539	81551	0011M	0005U	0021U	0113U	0228U
0339U	0343U	0359U	0403U	0424U	0433U			

Covered when medically necessary:

Procedure Codes								
81541	81542	0047U						

ICD-10 diagnosis codes:

ICD-10-CM Diagnosis Code	Description
C61	Malignant neoplasm of prostate
R97.21	Rising PSA following treatment for malignant neoplasm of prostate

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TOP

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IX. POLICY HISTORY

TOP

MP 2.280	**CAC 6/2/15 New policy adopting BCBSA** genetic and protein biomarkers for the diagnosis of prostate cancer are considered **investigational**: Policy coded.
	11/2/15 Administrative change. LCD number changed from L34796 to L35396 due to Novitas update to ICD-10.
	CAC 11/24/15 Medicare variation added to reference to Palmetto GBA Local Coverage Determination L35632 Confirm MDX Epigentic Molecular Assay. Coding updated.
	2/15/16 Administrative update. 2016 coding update, removed end dated code S3721.
	1/1/17 Administrative update. Product variation section reformatted. Added new code 81539 and removed end dated code 0010M; effective 1/1/17.
	CAC 11/29/16 Prostate Health Index (phi) added as an investigational test. LCD changed for ConfirmMDx to Noridian. Added new code 0005U for the ExosomeDx® Prostate test; effective 5/1/17.
	1/1/18 Administrative update. Added new code 81551 for Confirm MDx effective 1/1/18. Medicare variations removed from Commercial Policies.
	1/19/18 Administrative update. Added new code 0011M; effective 1/1/18
	1/5/18 Minor Review. Policy revised to separate initial biopsy and repeat biopsy populations. Prostarix test removed from policy. Policy Guidelines with genetics nomenclature update added. Coding reviewed.
	7/1/18 Administrative update. Added new code 0053U; effective 7/1/18**.**
	1/10/19 Minor review. The SelectMDx, ExoDx Prostate (IntelliScore), and Apifiny tests added as investigational. Rationale condensed and references updated. Coding updated.
	10/1/19 Coding update. New code 0113U added as investigational.
	10/2/19 Administrative update. Investigational test MiPS (Mi-Prostate Score) added to coordinate with add of new code 0113U.
	1/1/2020 Coding updated. Added new codes effective 1/1/2020: 81552, 81559, 0011M, 0005U, 0021U, 0053U, and 0113U.

	8/19/20 Consensus Review. No change in policy statement. Removed codes 81552 and 81559. Added Genetic counseling segment under policy guidelines. References and background updated.
	11/30/2020 Major review. Added medically necessary criteria for Gene expression profile analysis for the evaluation of prostate cancer based on NCCN Biomarker Compendium. Revised, statement, guidelines, references, and coding.
	12/29/2021 Minor review. Changed title of policy. Updated MN criteria for management of prostate cancer as well as policy guidelines. Updated FEP, Background, and references. Added code 81542 to MN coding table.
	8/29/2022 Minor review. Removed Promark as MN. Other management testing is now NMN. miR Sentinel™ test added to INV diagnosis tests. Updated guidelines, FEP, background, rationale, and references. Added 0228U, 0339U, and 0343U to INV coding table.
	12/1/2022 Administrative update. Added new code 0359U effective 1/1/23
	6/13/2023 Administrative update. Deleted 0053U effective 7/1/23
	9/7/2023 Administrative update. Added new code 0403U. Effective date 10/1/2023.
	12/12/2023 Administrative update. Added codes 0424U and 0433U.

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