Geisinger Health Plan Policies and Procedure Manual

Policy: MP273

Section: Medical Benefit Policy

Subject: Gene-based Testing and/or Protein Biomarkers for Diagnosis and Management of Prostate Cancer

Applicable line of business:

Commercial	**x**	**Medicaid**	**x**
Medicare	**x**	**ACA**	**x**
CHIP	**x**		

I. Policy: Gene-based Testing and/or Protein Biomarkers for Diagnosis and Management of Prostate Cancer

II. Purpose/Objective:

To provide a policy of coverage regarding Gene-based Testing and/or Protein Biomarkers for Diagnosis and Management of Prostate Cancer

III. Responsibility:

A. Medical Directors
B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

Commercial

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicare

Geisinger Gold Medicare Advantage HMO, PPO, and HMO D-SNP plans are offered by Geisinger Health Plan/Geisinger Indemnity Insurance Company, health plans with a Medicare contract. Continued enrollment in Geisinger Gold depends on contract renewal. Geisinger Health Plan/Geisinger Indemnity Insurance Company are part of Geisinger, an integrated health care delivery and coverage organization.

CHIP

Geisinger Health Plan Kids (GHP Kids) is a Children's Health Insurance Program (CHIP) offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicaid

Geisinger Health Plan Family (GHP Family) is a Medical Assistance (Medicaid) insurance program offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

DESCRIPTION:
Prostate cancer antigen 3 (PCA3, also referred to as DD3) is a gene that expresses a non-coding RNA. PCA3 is only expressed in human prostate tissue, and the gene is highly overexpressed in prostate cancer. Because of its restricted expression profile, the PCA3 RNA is thought to be useful as a tumor marker. The PCA3 Assay is an automated molecular assay that helps physicians determine the need for repeat prostate biopsies in members who have had a previous negative biopsy.

In vitro gene expression prognostic assays measure gene expression in tumor tissue samples or from prostate biopsy samples to provide a personalized risk score indicative of a tumor's aggressiveness and may also provide a long-range prostate cancer -specific mortality risk score.

Epigenetic assays utilize methylation-specific PCR to assess DNA methylation of gene regions that are associated with prostate cancer. The test assesses the methylation status of glutathione s-transferase PI (GSTP1), adenomatous polyposis coli (APC), and RAS association (RalGDS/AF-6) domain family member 1 (RASSF1).

Prolaris® is a genomic test developed to aid physicians in predicting prostate cancer aggressiveness in conjunction with clinical parameters such as Gleason score and PSA. Prolaris® is a direct molecular measure of prostate cancer tumor biology. By measuring the expression levels of genes involved with cancer replication, Prolaris® is promoted as being able to more accurately predict disease progression. Oncotype Dx® Prostate Cancer Assay (Genomic Health, Redwood City, CA) is a gene expression profiling test that uses archived tumor specimens as the mRNA source, and reverse transcriptase polymerase chain reaction (RT-PCR) amplification to quantify expression levels of 12 cancer-related and 5 reference genes to generate a Genomic Prostate Score. Decipher® is a 22 gene expression profile test intended to guide who can delay or defer radiation after radical prostatectomy. Promark™ is an automated quantitative imaging method to measure protein biomarkers by immunofluorescent staining in formalin-fixed paraffin-embedded biopsy tissue. It is designed to provide prognostic information to help differentiate patients to active surveillance or therapy.

The National Comprehensive Cancer Network® (NCCN) guidelines for prostate cancer (v 1.2018) encourages physicians to consider molecular testing of a patient's tumor post-biopsy when prostate cancer presents as low- or favorable intermediate-risk and life expectancy is greater than or equal to 10 years.

COMMERCIAL and NON-MEDICARE BUSINESS SEGMENTS

ConfirmMDx (81551) is covered for members with negative or non-malignant abnormal histopathology findings, such as atypical cell or high-grade prostate intraepithelial neoplasia (HGPIN) on prostate biopsy, yet with high-risk factors (elevated/rising PSA or abnormal digital rectal exam) and are candidates for repeat biopsy

SelectMDx (0339U) is covered when **all of the following** criteria are met:

1. The member is a candidate for prostate biopsy or repeat prostate biopsy, (NCCN criteria):
    - For men ≤ 75 years of age - Prostate Specific Antigen (PSA) (or adjusted PSA in special populations, i.e., patients taking 5alpha-reductase inhibitors) OR repeat PSA are >3 and <10ng/mL AND/OR Digital Rectal Exam (DRE) findings are very suspicious for cancer; **or**
    - For men > 75 years of age - PSA (or adjusted PSA in special populations, i.e., patients taking 5alpha-reductase inhibitors) OR repeat PSA are ≥4 and <10ng/mL AND/OR DRE findings are very suspicious for cancer

and

2. The member has not had a prostate biopsy OR has had a previous negative or non-malignant but abnormal histopathology finding (i.e., atypical small acinar proliferation or high-grade prostatic intraepithelial neoplasia (HGPIN) on prostate biopsy); **or**
   Member is under consideration for a repeat biopsy have first undergone repeat PSA and/or DRE testing AND a repeat biopsy is considered within 24-months of the prior biopsy.

and

3. The test is ordered by a physician specialist in the management of prostate cancer, such as a urologist or oncologist.

Prolaris, Oncotype Dx Prostate, Decipher: (81541, 81542, 0047U)
Gene expression prognostic assay (eg, **Prolaris, Oncotype Dx Prostate, Decipher**) is covered for members to help determine which members with early stage, needle biopsy proven prostate cancer can be conservatively managed rather than treated with definitive surgery or radiation therapy when **all of the following** criteria are met:

1. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), **and**
2. Formalin fixed paraffin-embedded (FFPE) prostate biopsy specimen with at least 0.5 mm of cancer length; **and**
3. Stage as defined by the one of the following:
    • Very Low Risk Disease (T1c AND Gleason Score ≤ 6 AND PSA ≤ 10 ng/mL AND <3 prostate cores with tumor AND ≤ 50% cancer in any core AND PSA density of < 0.15 ng/mL/g) **OR**
    • Low Risk Disease (T1-T2a AND Gleason Score ≤ 6 AND PSA ≤ 10 ng/mL), **and**
4. The member has an estimated life expectancy of greater than or equal to 10 years, **and**
5. The member is a candidate for and is considering conservative therapy and yet would be eligible for definitive therapy (radical prostatectomy, radiation therapy or brachytherapy), **and**
6. Result will be used to determine treatment between definitive therapy and conservative management.

OncoType DX AR-V7 assay is covered when **all of the following** criteria are met:

1. The member is diagnosed with progressive mCRPC as defined by the Prostate Cancer Working Group 2 guidelines (a minimum of 2 rising prostate-specific antigen (PSA) levels 1 or more weeks apart, new lesions by bone scintigraphy, and/or new or enlarging soft tissue lesions by computed tomography or magnetic resonance imaging; **and**

2. The member has experienced failure on one androgen receptor signaling inhibitor (ARSi), (e.g., Enzalutamide (Xtandi), Apalutamide (Erleada), or Abiraterone (Zytiga).; **and**
3. The member is considered to be appropriate for treatment by their treating physician for the alternative ARSi as a single agent; **and**
4. Circulating tumor cells with nuclear expression of AR-V7 protein will be assessed prior to initiation of therapy

4Kscore (0011M, 81539) testing will be considered for coverage when **all of the following** criteria are met:

A. The member is 45 years of age and older, prior to an initial biopsy or following a negative biopsy, who has a confirmed moderately elevated PSA defined as greater than 3 and less than 10 ng/mL; **or**

B. The member is 75 years of age and older, prior to an initial biopsy or following a negative biopsy, who has a confirmed moderately elevated PSA defined as greater than or equal to 4 and less than 10 ng/mL

and **BOTH** of the following are present:

1. No other relative indication for prostate biopsy including **ANY** of the following: (this may not be an all-inclusive list):
    - DRE suspicious for cancer should be encouraged to undergo biopsy
    - Persistent and significant increase in PSA should be encouraged to undergo biopsy
    - Positive multiparametric magnetic resonance imaging (MRI) (if done)
    - Other major risk factor for prostate cancer including: (this may not be an all-inclusive list)
        - Ethnicity at higher risk for prostate cancer
        - First-degree relative with prostate cancer
        - High-penetrance prostate cancer risk gene(s) per the National Comprehensive Cancer Network (NCCN) (if known)

2. No other relative contraindication for prostate biopsy including **ANY** of the following:
    - Less than a 10 year life expectancy
    - Benign disease not ruled out.

MyProstateScore (0403U) testing will be considered for coverage when all of the following criteria are met:
- The member is a candidate for initial or repeat prostate biopsy; and.
- The member does not have a diagnosis of prostate cancer; and
- PSA is ≥ 3 ng/mL AND/OR digital rectal exam findings are very suspicious for cancer.

IsoPSA (0359U) testing will be considered for coverage when all of the following criteria are met:
- The member is a candidate for initial or repeat prostate biopsy; and.
- The member does not have a diagnosis of prostate cancer; and
- PSA is ≥ 3 ng/mL AND/OR digital rectal exam findings are very suspicious for cancer.

MEDICARE BUSINESS SEGMENT:

PCA3 Assay (eg, Progensa (81313)) is covered for members to help determine the need for repeat prostate biopsies in members who have had a previous negative biopsy.

ConfirmMDx (81551)
Palmetto GBA a Medicare Administrative Contractor (MAC) that assesses molecular diagnostic technologies and establishes the coverage policy for Medicare beneficiaries has determined that **ConfirmMDx** is covered in members with previous negative prostate biopsy who are being considered for repeat biopsy when the following criteria are met:
- 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
- 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
- Minimum tissue volume criteria of 20 microns of prostate biopsy core tissue is available (40 microns preferable), and
- 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
- Member is not being managed by active surveillance for low stage prostate cancer, and
- Tissue was extracted using standard patterned biopsy core extraction (and not transurethral resection of the prostate (TURP)), and
- Member has not been previously tested by ConfirmMDx from the same biopsy samples or similar molecular test

Decipher Biopsy Prostate Cancer Classifier Assay (81542)
Palmetto GBA a Medicare Administrative Contractor (MAC) that assesses molecular diagnostic technologies and establishes the coverage policy for Medicare beneficiaries has determined that **Decipher Biopsy Prostate Cancer Classifier Assay** is covered for Men with Favorable Intermediate Risk Disease and with Unfavorable Intermediate Risk Disease when the following criteria are met:

A. Favorable Intermediate Risk Disease Criteria:

- Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), **and**
- FFPE prostate biopsy specimen with at least 0.5 mm of cancer length, and favorable intermediate risk disease defined as:
    - Gleason Grade Group 2 (Gleason Sum 3+4=7); **and**
    - Estimated life expectancy of greater than or equal to 10 years, **and**
- Member is a candidate for and is considering conservative management and yet would be eligible for definitive therapy (radical prostatectomy, radiation or brachytherapy), **and**
- Result will be used to determine treatment between definitive therapy and conservative management, **and**
- Member has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, **and**
- Member is monitored for disease progression according to established standard of care

B. <u>Unfavorable Intermediate Risk Disease Criteria</u>:

- Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), **and**
- FFPE prostate biopsy specimen with at least 0.5 mm of cancer length, and unfavorable risk disease defined as:
    - Gleason score 3+4=7 / grade group 2 or Gleason score 4+3=7 / grade group 3, **or**
    - T2b to T2c, **or**
    - PSA 10-20 ng/mL, **and**
- Estimated life expectancy of greater than or equal to 10 years, **and**
- Member is a candidate for definitive therapy (RP +/- PLND, EBRT + ADT, or EBRT + brachytherapy +/- ADT), **and**
- Result will be used to determine treatment between definitive therapy modality, **and**
- Member has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, **and**
- Member is monitored for disease progression according to established standard of care

Prolaris, ProMark, Oncotype Dx Prostate (81541,0047U)

Gene expression prognostic assay (eg, **Prolaris, ProMark, Oncotype Dx Prostate**) is covered for members to help determine which members with early stage, needle biopsy proven prostate cancer can be conservatively managed rather than treated with definitive surgery or radiation therapy.

Palmetto GBA a Medicare Administrative Contractor (MAC) that assesses molecular diagnostic technologies and establishes the coverage policy for Medicare beneficiaries has determined that **Prolaris** testing will be considered for coverage when the following criteria are met:

1. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), **and**
2. Formalin fixed paraffin-embedded (FFPE) prostate biopsy specimen with at least 0.5 mm of cancer length, **and**
3. Member Stage as defined by the one of the following:
    - Very Low Risk Disease (T1c AND Gleason Score ≤ 6 AND PSA ≤ 10 ng/mL AND <3 prostate cores with tumor AND ≤ 50% cancer in any core AND PSA density of < 0.15 ng/mL/g) **OR**
    - Low Risk Disease (T1-T2a AND Gleason Score ≤ 6 AND PSA ≤ 10 ng/mL), and
4. Member has an estimated life expectancy of greater than or equal to 10 years, **and**
5. Member is a candidate for and is considering conservative therapy and yet would be eligible for definitive therapy (radical prostatectomy, radiation therapy or brachytherapy), **and**
6. Result will be used to determine treatment between definitive therapy and conservative management, **and**
7. Member has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, **and**
8. Test is ordered by a physician certified in the Myriad Prolaris™ Certification and Training Registry (CTR), **and**
9. Member is monitored for disease progression according to established standard of care, **and**
10. Physician must report the development of metastasis or prostate cancer deaths in members not treated definitively who were deemed low risk by the assay.

OncoType DX AR-V7

Palmetto GBA a Medicare Administrative Contractor (MAC) that assesses molecular diagnostic technologies and establishes the coverage policy for Medicare beneficiaries has determined that **OncoType DX AR-V7** assay is covered when the following criteria are met:

1. The member is diagnosed with progressive mCRPC as defined by the Prostate Cancer Working Group 2 guidelines (a minimum of 2 rising prostate-specific antigen (PSA) levels 1 or more weeks apart, new lesions by bone scintigraphy, and/or new or enlarging soft tissue lesions by computed tomography or magnetic resonance imaging; and
2. The member has experienced failure on one androgen receptor signaling inhibitor (ARSi), (e.g., Enzalutamide (Xtandi), Apalutamide (Erleada), or Abiraterone (Zytiga).; and
3. The member is considered to be appropriate for treatment by their treating physician for the alternative ARSi as a single agent; and
4. Circulating tumor cells with nuclear expression of AR-V7 protein will be assessed prior to initiation of therapy

4Kscore (0011M, 81539)

Palmetto GBA a Medicare Administrative Contractor (MAC) that assesses molecular diagnostic technologies and establishes the coverage policy for Medicare beneficiaries has determined that **4Kscore** testing will be considered for coverage when the following criteria are met:

C. The member is 45 years of age and older, prior to an initial biopsy or following a negative biopsy, who has a confirmed moderately elevated PSA defined as greater than 3 and less than 10 ng/mL; **or**

D. The member is 75 years of age and older, prior to an initial biopsy or following a negative biopsy, who has a confirmed moderately elevated PSA defined as greater than or equal to 4 and less than 10 ng/mL

and **BOTH** of the following are present:

3. No other relative indication for prostate biopsy including **ANY** of the following: (this may not be an all inclusive list):
   - DRE suspicious for cancer should be encouraged to undergo biopsy
   - Persistent and significant increase in PSA should be encouraged to undergo biopsy
   - Positive multiparametric magnetic resonance imaging (MRI) (if done)
   - Other major risk factor for prostate cancer including: (this may not be an all inclusive list)
     - Ethnicity at higher risk for prostate cancer
     - First-degree relative with prostate cancer
     - High-penetrance prostate cancer risk gene(s) per the National Comprehensive Cancer Network (NCCN) (if known)

4. No other relative contraindication for prostate biopsy including **ANY** of the following:
   - Less than a 10 year life expectancy
   - Benign disease not ruled out.

Select MDX (0339U)

1. The member is a candidate for prostate biopsy or repeat prostate biopsy, (NCCN criteria):
   - For men ≤ 75 years of age - Prostate Specific Antigen (PSA) (or adjusted PSA in special populations, i.e., patients taking 5alpha-reductase inhibitors) OR repeat PSA are >3 and <10ng/mL AND/OR Digital Rectal Exam (DRE) findings are very suspicious for cancer; **or**
   - For men > 75 years of age - PSA (or adjusted PSA in special populations, i.e., patients taking 5alpha-reductase inhibitors) OR repeat PSA are ≥4 and <10ng/mL AND/OR DRE findings are very suspicious for cancer

and

2. The member has not had a prostate biopsy OR has had a previous negative or non-malignant but abnormal histopathology finding (i.e., atypical small acinar proliferation or high-grade prostatic intraepithelial neoplasia (HGPIN) on prostate biopsy); **or**
   Member is under consideration for a repeat biopsy have first undergone repeat PSA and/or DRE testing AND a repeat biopsy is considered within 24-months of the prior biopsy.

and

3. The test is ordered by a physician specialist in the management of prostate cancer, such as a urologist or oncologist.

ExoDx Prostate (IntelliScore) (0005U)

1. The member is age > 50 years of age; and
2. The test will be performed prior to an initial prostate biopsy; or
3. The individual has had a prior negative prostate biopsy; and
4. There is continued clinical suspicion of prostate cancer based on elevation of prostate specific antigen (PSA) >3 ng/mL, and for whom an initial prostate biopsy or repeat prostate biopsy would be recommended by a urologist based on current standard of care.

MyProstateScore (0403U) testing will be considered for coverage when all of the following criteria are met:

- The member is a candidate for initial or repeat prostate biopsy; and.
- The member does not have a diagnosis of prostate cancer.
    - For men ≤ 75 years of age, PSA is ≥ 3 ng/mL AND/OR digital rectal exam findings are very suspicious for cancer.
    - For men > 75 years of age, PSA is ≥ 4 ng/mL AND/OR digital rectal exam findings are very suspicious for cancer.

IsoPSA (0359U) testing will be considered for coverage when all of the following criteria are met:

- The member is a candidate for initial or repeat prostate biopsy; and.
- The member does not have a diagnosis of prostate cancer; and
- PSA is ≥ 3 ng/mL AND/OR digital rectal exam findings are very suspicious for cancer.

MEDICAID BUSINESS SEGMENT:

PA Dept. of Human Services has determined the 4K Score test (81539) is considered to be experimental/Investigational and therefore **NOT COVERED. A Program Exception request is required.**

PA Dept. of Human Services has determined gene expression prognostic assay Prolaris is considered to be experimental/Investigational and therefore **NOT COVERED.**

PA Dept. of Human Services has determined PCA/KLK3 is considered to be experimental/Investigational and therefore **NOT COVERED**.

PA Dept. of Human Services has determined Oncotype DX Prostate Cancer Assay is considered to be experimental/Investigational and therefore **NOT COVERED**.

Medicaid Business Segment:

Any requests for services that do not meet criteria set in the PARP may be evaluated on a case by case basis.

EXCLUSIONS:

Unless coverage is mandated, the Plan considers Promark™, Apifiny, PanGIA Prostate, miR Sentinel Prostate Test, and Episwitch Prostate Screening Test **to be unproven** for all indications including, but not limited to, the aid in predicting prostate cancer aggressiveness. There is insufficient evidence in the peer-reviewed published medical literature to establish the effectiveness of this test on health outcomes when compared to established tests or technologies. **(0021U, 0113U, 0228U, 0343U, 0424U, 0433U)**

The Geisinger Technology Assessment Committee determined that at the present time, there is insufficient evidence in the peer-reviewed, published medical literature to support the use of PCA3 assay to determine the need for repeat biopsy in members who have had a previous negative prostate biopsy. Unless mandated by state or federal regulation, this testing is currently considered to be **experimental, investigational or unproven**, and therefore **NOT COVERED**.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

CODING ASSOCIATED WITH: Gene-based Testing and/or Protein Biomarkers for Diagnosis and Management of Prostate Cancer

The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov ***or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.***

81313 PCA3 (prostate cancer antigen 3/ kallikrein-related peptidase 3) {Progensa}
81479 Unlisted procedure
81539 Oncology (high grade prostate cancer), biochemical assay of four proteins (total PSA, free PSA, intact PSA and kallikrein-2) utilizing plasma or serum, prognostic algorithm reported as a probability score {4Kscore}
81541 Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score {Prolaris}
81542 Oncology (prostate), mRNA , microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score {Decipher®, Decipher® Prostate Cancer Assay or Decipher® Prostate Cancer Classifier}
81551 Oncology (prostate), promoter methylation profiling by real-time PCR of 3 genes (GSTP1, APC, RASSF1), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a likelihood of prostate cancer detection on repeat biopsy [Confirm MDx}
88387 Macroscopic examination, dissection, and preparation of tissue for non-microscopic analytical studies (e.g., nucleic acid-based molecular studies); each tissue preparation (e.g., a single lymph node)
88363 Examination and selection of retrieved archival (i.e., previously diagnosed) tissue(s) for molecular analysis (e.g., KRAS mutational analysis)
0005U Oncology (prostate) gene expression profile by real time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine algorithm reported as risk score {ExoDx Prostate} {IntelliScore}/ExosomeDx Prostate {IntelliScore}
0011M Oncology, prostate cancer, mRNA expression assay of 12 genes (10 content and 2 housekeeping), RT-PCR test utilizing blood plasma and/or urine, algorithms to predict high grade cancer risk {4Kscore Test}
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 *{Apifiny}*
0047U Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score {OncoType Dx Prostate}
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 *{MyProstateScore}*
0228U Oncology (prostate), multianalyte molecular profile by photometric detection of macromolecules adsorbed on nanosponge array slides with machine learning, utilizing first morning voided urine, algorithm reported as likelihood of prostate cancer *{PanGIA Prostate}*
0339U Oncology (prostate), mRNA expression profiling of HOXC6 and DLX1, reverse transcription polymerase chain reaction (RT-PCR), first-void urine following digital rectal examination, algorithm reported as probability of high-grade cancer *{SelectMDx for Prostate Cancer}*
0343U Oncology (prostate), exosome-based analysis of 442 small noncoding RNAs (sncRNAs) by quantitative reverse transcription polymerase chain reaction (RT-qPCR), urine, reported as molecular evidence of no-, low-, intermediate- or high-risk of prostate cancer. *{miR Sentinel Prostate Cancer Test}*
0359U Oncology (prostate cancer), analysis of all prostate-specific antigen (PSA) structural isoforms by phase separation and immunoassay, plasma, algorithm reports risk of cancer *{IsoPSA}*
0403U Oncology (prostate), mRNA, gene expression profiling of 18 genes, first-catch post-digital rectal examination urine (or processed first-catch urine), algorithm reported as percentage of likelihood of detecting clinically significant prostate cancer *{ MyProstateScore 2.0}*
0424U Oncology (prostate), exosome-based analysis of 53 small noncoding RNAs (sncRNAs) by quantitative reverse transcription polymerase chain reaction (RT-qPCR), urine, reported as no molecular evidence, low-, moderate- or elevated-risk of prostate cancer {*miR Sentinel Prostate Test}*
0433U Oncology (prostate), 5 DNA regulatory markers by quantitative PCR, whole blood, algorithm, including prostate-specific antigen, reported as likelihood of cancer *{Episwitch Prostate Screening Test}* New 2024

0495U Oncology (prostate), analysis of circulating plasma proteins (tPSA, fPSA, KLK2, PSP94, and GDF15), germline polygenic risk score (60 variants), clinical information (age, family history of prostate cancer, prior negative prostate biopsy), algorithm reported as risk of likelihood of detecting clinically significant prostate cancer

0497U Oncology (prostate), mRNA gene-expression profiling by real-time RT-PCR of 6 genes (FOXM1, MCM3, MTUS1, TTC21B, ALAS1, and PPP2CA), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a risk score for prostate cancer

0512U Oncology (prostate), augmentative algorithmic analysis of digitized whole-slide imaging of histologic features for microsatellite instability (MSI) status, formalin-fixed paraffin-embedded (FFPE) tissue, reported as increased or decreased probability of MSI-high (MSI-H)

0513U Oncology (prostate), augmentative algorithmic analysis of digitized whole-slide imaging of histologic features for microsatellite instability (MSI) and homologous recombination deficiency (HRD) status, formalin-fixed paraffin-embedded (FFPE) tissue, reported as increased or decreased probability of each biomarker

LINE OF BUSINESS:

Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:

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MolDx A59220 Response to Comments: Biomarker Testing for Prostate Cancer Diagnosis

This policy will be revised as necessary and reviewed no less than annually.

Devised: 3/13

Revised: 2/15 (add Medicare & Medicaid coverage), 2/18 (title change, added clinical information); 8/18 (added exclusion for Medicaid) 8/19 (add coverage); 1/20 (add Decipher coverage; 4Kscore coverage for Medicare); 2/21 (add Medicaid Exclusions); 1/22 (add SelectMDx and 4K for Commercial) 7/22 (add select MDx for Medicare); 7/23 (add ExoDx,); 7/24 (Add exclusions for MyProstateScore, Apifiny, PanGIA Prostate,IsoPSA, miR Sentinel Prostate Test, and Episwitch Prostate Screening Test as Unproven); 11/24 (add coverage for MyProstateScore and IsoPSA)

Reviewed: 3/14**,** 2/16, 2/17

CMS UM Oversight Committee Approval: 12/23, 7/24 ,12/24