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

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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.

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

Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

(i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.

(ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.

(iii) The service or benefit 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 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

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

MEDICARE BUSINESS SEGMENT:

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

Gene expression prognostic assay (eg, Prolaris, ProMark, OncoType Dx) is covered for members to help determine which patients 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. Patient 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. Patient has an estimated life expectancy of greater than or equal to 10 years, **and**
5. Patient 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. Patient 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. Patient 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 patients not treated definitively who were deemed low risk by the assay.

MEDICAID BUSINESS SEGMENT:

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

EXCLUSIONS:
Unless coverage is mandated, the Plan considers Decipher® and Promark™ **experimental**, **investigational, and 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.

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
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}

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)
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}

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.

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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)

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