Genetic Testing for Prostate Cancer

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Disclaimer
Refer to the member’s specific benefit plan and Schedule of Benefits to determine coverage. This may not be a benefit on all plans or the plan may have broader or more limited benefits than those listed in these criteria.

Prior Authorization is required. Please use the Prior Authorization/Benefit Certification Guide to determine when a prior authorization/benefit certification is required https://ds.phs.org/preslogin/index.jsp

Description

Diagnostic Testing:
I. 4Kscore Test Algorithm
II. Progensa® PCA3 Assay:
III. BRCA1 and BRCA2 Genetic Testing:
IV. ConfirmMDx Epigenetic Molecular Assay:

Treatment/management Testing:
I. Decipher® Prostate Cancer Classifier Assay Test:
II. Decipher Biopsy Prostate Cancer Classifier Assay for Men with NCCN Low Risk and Very Low Risk Prostate Cancer:
III. Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Intermediate Risk Disease
IV. Oncotype DX AR-V7 Nucleus Detect for Men with Metastatic Castrate Resistant Prostate Cancer (MCRPC):
V. Genomic Health™ Oncotype DX® Prostate Cancer Assay:
VI. Oncotype DX® Genomic Prostate Score for Men with Favorable Intermediate Risk Prostate Cancer:
VII. Prolaris™ Prostate Cancer Genomic Assay:
VIII. Prolaris™ Prostate Cancer Genomic Assay for Men with Favorable Intermediate Risk Disease:
IX. ProMark Risk Score:

Coverage Determination for Medicare

Diagnostic Testing:
I. 4Kscore Test Algorithm:
   For Medicare members only. Not a covered benefit for Centennial and Commercial members.

   For purpose of criteria PHP follows CMS 4Kscore Test Algorithm, LCD (L37792) and Policy Article A56653. The 4Kscore test will be considered medically reasonable and necessary when all the following are met:

   1. When all of the components of the algorithm are present.

Not every Presbyterian health plan contains the same benefits. Please refer to the member’s specific benefit plan and Schedule of Benefits to determine coverage. [MPMPPC051001]
2. Testing of men 45 years of age and older, prior to an initial biopsy or following a negative biopsy, who have a **confirmed*** moderately elevated PSA (greater than 3 and less than 10 ng/mL; greater than or equal to 4 and less than 10 ng/mL in men greater than 75 years of age) when BOTH of the following are present:
   - 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:
       - 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)
   - No other relative **contraindication** for prostate biopsy including ANY of the following:
     - Less than a 10 year life expectancy
     - Benign disease not ruled out.

II. **Progensa® PCA3 Assay**:

   **For Medicare members only. Not a covered benefit for Centennial and Commercial members.**

   For purpose of criteria PHP follows CMS MolDX: Molecular Diagnostic Tests (MDT), LCD L36807 with related Policy Article (A55202); Biomarkers for Oncology, LCD L35396 with related Policy Article (A52986). The PROGENSA® PCA3 Assay (PRED) helps physicians determine the need for repeat prostate biopsies in men who have had a previous negative biopsy. An mRNA expression assay is used alone or in combination with other molecular tests for prostate cancer determination, such as RSA for those patients with high risk of prostate cancer.

   FDA approved testing of PCA3 Assay is covered **ONLY** when all biopsies in previous encounter(s) are negative and when the patient or physician wants to avoid repeat biopsy (watchful waiting).

   **NOTE:** When the physician already plans to biopsy the prostate, PHP will consider a PCA3 test as investigational and thus, not a
III. BRCA1 and BRCA2 Genetic Testing:

For Centennial and Commercial members: PHP follows the current version NCCN guidelines. (For Medicare members please see below section).

For Medicare members:
For purpose of criteria PHP follows WPS MolDX: BRCA1 and BRCA2 Genetic Testing, LCD (L36813) with related Policy Articles (A57771) and (A55224); BRCA1 and BRCA2 Genetic Testing by Novitas (L36715), with related Article (A56542). Please review each LCDs for criteria.

BRCA testing limited to once-in-a-lifetime.

Genetic screening in the general population or when individuals with no personal history of breast, primary peritoneal, pancreatic, or prostate cancer, such testing is considered screening and is not covered.

Testing for BRCA 1 and BRCA 2 genes for patients suspected of hereditary breast and/or ovarian cancer syndromes. The individual being tested must have signs or symptoms of breast cancer [invasive or ductal carcinoma in situ (DCIS)], primary peritoneal cancer, pancreatic cancer, or prostate cancer and meet one of the criteria below. Genetic testing for a known mutation in a family is a covered service for individuals with signs and/or symptoms of cancer. Testing of an unaffected individual or family member is not a covered benefit.

Criteria for Testing

A. The following indications for BRCA1/2 are covered:

- Individual with breast, pancreatic, or prostate cancer from a family with a known deleterious BRCA1 or BRCA2 gene mutation.

- Individual with male breast cancer.

- Personal history of high-grade prostate cancer (Gleason score greater than or equal to 7) at any age with:
  - \( \geq 1 \) first, second, or third degree relative\(^2\) with ovarian cancer at any age, or
  - \( \geq 1 \) first, second, or third degree relative\(^2\) with breast cancer \( \leq 50 \) y, or
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- ≥1 first, second, or third degree relative with pancreatic cancer at any age, or
- ≥1 first, second, or third degree relative with metastatic prostate cancer pancreatic cancer at any age, or
- ≥2 first, second, or third degree relatives with breast cancer and/or pancreatic cancer and/or prostate cancer (any grade) at any age, or
- Ashkenazi Jewish ancestry
  - Personal history of pancreatic cancer at any age
  - Personal history of metastatic prostate cancer (radiographic evidence of or biopsy-proven disease)
  - BRCA1/2 pathogenic mutation detected by tumor profiling on any tumor type in the absence of germline mutation analysis.

IV. ConfirmMDx Epigenetic Molecular Assay:

For Medicare members only. Not a covered benefit for Centennial and Commercial members.

For purpose of criteria PHP follows CMS, MolDX: ConfirmMDx Epigenetic Molecular Assay LCD (L37005), with related Policy Article (A57561). Limited coverage for the ConfirmMDx epigenetic assay for prostate cancer so to reduce unnecessary repeat prostate biopsies.

A. 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

B. 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 Formalin-Fixed, Paraffin-Embedded (FFPE) tissue from all cores is available for testing, and

C. Minimum tissue volume criteria of 20 microns of prostate biopsy core tissue is available (40 microns preferable), and

D. 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),

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and

E. Patient is not being managed by active surveillance for low stage prostate cancer, and

F. Tissue was extracted using standard patterned biopsy core extraction (and not transurethral resection of the prostate (TURP), and

G. Patient has not been previously tested by ConfirmMDx from the same biopsy samples or similar molecular test.

**Treatment/management Testing:**

I. **Decipher® Prostate Cancer Classifier Assay Test:**

For Medicare members only. Not a covered benefit for Centennial and Commercial members.

For purpose of criteria PHP follows CMS MolDX: Decipher® Prostate Cancer Classifier Assay LCD (L36791) with related Policy Article (A57565) is covered only when the following conditions are met:

A. Patient with prostate cancer who has undergone a Radical Prostatectomy (RP) with in the previous 5 yrs (60 months) and is being considered for postoperative secondary therapy due to one or cancer-recurrence risk factors, and

B. Patient must have achieved initial PSA nadir (defined as PSA at or below 0.2ng/ml) within 120 days of RP surgery, and

C. Patient must not have any evidence of distant metastasis, and

D. Patient must not have received any neo-adjuvant treatment prior to surgery, and

E. Decipher GC is performed on a patient's RP specimen, and

F. Patient’s surgical pathology report or medical records must have documented presence of adverse pathology:
   - Pathological stage T2 disease with a positive surgical margin, or Patient’s surgical pathology report or medical records must have documented presence of adverse pathology:
   - Pathological stage T3 disease (e.g., extraprostatic extension, seminal vesicle invasion, bladder neck
invasion), or
  o Rising PSA after initial PSA nadir, and

G. Testing has been ordered by a physician who is certified in the Decipher Biosciences Certification and Training Registry (CTR). See LCD for details on CTR.

II. Decipher Biopsy Prostate Cancer Classifier Assay for Men with NCCN Low Risk and Very Low Risk Prostate Cancer:

For Medicare members only. Not a covered benefit for Centennial and Commercial members

For purpose of criteria PHP follows CMS MolDX: Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Disease, LCD (L37911) with related Policy Article A57564 when the following conditions are met:

A. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), and

B. Formalin-Fixed, Paraffin-Embedded (FFPE) prostate biopsy specimen with at least 0.5 mm of cancer length, and

C. Patients with low risk or very low risk as defined by the NCCN as follows:

1. Low Risk:
   o Stage T1 or T2a
   o PSA less than 10 ng/mL
   o Gleason score 6 or less (Grade Group 1) OR

2. Very Low Risk: Stage T1c
   o PSA less than 10 ng/mL
   o Gleason score 6 or less (grade group 1)
   o Not more than two cores with cancer
   o Less than or equal to 50 percent of core involved with cancer
   o PSA density less than 0.15

D. Patient has an estimated life expectancy of greater than or equal to 10 years, and

E. 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
F. Result will be used to determine treatment between definitive therapy and conservative management by active surveillance (AS) and

G. Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and

H. Patient is monitored for disease progression based on the established standard of care, including at least a repeat biopsy at 1 year.

III. Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Intermediate Risk Disease

For Medicare members only. Not a covered benefit for Centennial and Commercial members

For purpose of criteria PHP follows CMS MolDX: Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Intermediate Risk Disease, LCD (L38166) with related Policy Article (A57798), when the following conditions are met.

The Decipher Biopsy test is covered for men with prostate cancer only when the following clinical conditions are met:

- 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 or unfavorable intermediate risk disease as defined in the most recent available NCCN guideline 2018 V4, and

- Patient has an estimated life expectancy of greater than or equal to 10 years, and

- Patient is a candidate for definitive therapy (RP +/- PLND, EBRT + ADT, or EBRT + brachytherapy +/- ADT), and

- Result will be used to determine treatment among definitive therapy modalities or observation, and

- Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and

- Patient is monitored for disease progression according to established standard of care

Variants of the Decipher Biopsy test including the genes / transcripts or algorithms are also covered for the above indications if those variations have analytical and clinical validity at
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IV. Oncotype DX AR-V7 Nucleus Detect for Men with Metastatic Castrate Resistant Prostate Cancer (MCRPC):

For Medicare members only. Not a covered benefit for Centennial and Commercial members

For the purpose of criteria PHP follows CMS MolDX: Oncotype DX AR-V7 Nucleus Detect for Men with Metastatic Castrate Resistant Prostate Cancer (MCRPC), LCD (L37915) with related Policy Article (A57582). The test helps to determine which patients with metastatic castrate resistant prostate cancer may benefit from androgen receptor signaling inhibitor (ARSi) therapy and which may benefit from chemotherapy.

Oncotype DX AR-V7 Nuclear Detect assay is covered as follows:

A. Patients will have 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 (CT) or magnetic resonance imaging (MRI)).

B. Patients will have failed one ARSi, specifically Enzalutamide (Xtandi), Apalutamide (Erleada), or Abiraterone (Zytiga).

C. Patients will be considered appropriate for treatment by their treating physician for the alternative ARSi as a single agent.

D. Circulating tumor cells (CTC) with nuclear expression of AR-V7 protein will be assessed prior to initiation of therapy.

E. Decision impact analysis: We expect that <15% of nuclear AR-V7-positive patients will receive an ARSi.

F. Efficacy analysis: Nuclear AR-V7-negative patients who receive an ARSi will have similar or better time on therapy than untreated mCRPC patients (meeting above criteria) receiving ARSi.

V. Genomic Health™ Oncotype DX® Prostate Cancer Assay:

A covered benefit for Medicare, Centennial and Commercial.

For the purpose of criteria PHP follows CMS MolDX: Genomic Health™ Oncotype DX® Prostate Cancer Assay, LCD (L36789) and related Policy Article (A56334). The test helps determine which
patients with early stage, needle biopsy proven prostate cancer, can be conservatively managed rather than treated with definitive surgery or radiation therapy.

Oncotype DX® prostate cancer assay is covered only when the following clinical conditions are met:

A. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), and

B. 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/OR Low Risk Disease (T1-T2a AND Gleason Score = 6 AND PSA = 10 ng/mL), Patient has an estimated life expectancy of ≥ 10 years, and

C. Patient has a life expectancy of 10-20 years,

D. Patient is a candidate for and is considering conservative therapy and would be eligible for definitive therapy (radical prostatectomy, radiation therapy or brachytherapy), and

E. Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and

F. Test is ordered by a physician certified in the Genomic Health™ Oncotype DX® Prostate Cancer Assay Certification and Training Registry (CTR) (see LCD for details) and

G. Patient is monitored for disease progression according to active surveillance guidelines as recorded in NCCN guidelines, and

H. Physician must report the development of metastasis or prostate cancer deaths in patients not treated definitively who were deemed low risk by the assay.

VI. Oncotype DX® Genomic Prostate Score for Men with Favorable Intermediate Risk Prostate Cancer:

A covered benefit for Medicare, Centennial and Commercial members.

For purpose of criteria PHP follows CMS MolDX: Oncotype DX® Genomic Prostate Score for Men with Favorable Intermediate Risk Prostate Cancer, LCD (L37667) with related Policy Article (A56334). Oncotype DX® Genomic Prostate Score (Genomic Health®) (hereafter GPS) test help determine which patients with favorable intermediate-risk, needle biopsy proven prostate cancer,
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can be conservatively managed rather than treated with definitive surgery or radiation therapy.

Oncotype DX Genomic Prostate Score test is covered for men with favorable intermediate risk prostate cancer only when the following clinical conditions are met:

A. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), and
B. Formalin-Fixed, Paraffin-Embedded (FFPE) prostate biopsy specimen with at least 0.5 mm of cancer length, and NCCN Favorable Intermediate-risk disease defined as:
   o Gleason Grade Group 2 (Gleason Sum 3+4=7), and
C. Patient has an estimated life expectancy of greater than or equal to 10 years, and
D. 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
E. Result will be used to determine treatment between definitive therapy and conservative management, and
F. Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and Patient is monitored for disease progression according to established standard of care.

VII. Prolaris™ Prostate Cancer Genomic Assay:

For Medicare members only. Not a covered benefit for Centennial and Commercial members.

For purpose of criteria PHP follows CMS MolDX: Prolaris™ Prostate Cancer Genomic Assay, LCD (L36787) with related Policy Article (A57585). This test help to determine which patients with early stage, needle biopsy proven Prostate Cancer, can be conservatively managed rather than treated with definitive surgery or radiation therapy.

Prolaris™ Assay is covered only when the following clinical conditions are met:

A. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), and
B. Formalin-Fixed, Paraffin-Embedded (FFPE) prostate biopsy
specimen with at least 0.5 mm of cancer length, and
C. Patient stage as defined by 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), Patient has an estimated life
     expectancy of ≥ 10 years, and
D. Patient has an estimated life expectancy of greater than or
   equal to 10 years, and
E. Patient is a candidate for and is considering conservative
   therapy and yet and would be eligible for definitive therapy
   (radical prostatectomy, radiation therapy or brachytherapy),
   and
F. Result will be used to determine treatment between
   definitive therapy and conservative management, and
G. Patient has not received pelvic radiation or androgen
   deprivation therapy prior to the biopsy, and
H. Test is ordered by a physician certified in the in the Myriad
   Prolaris™ Certification and Training Registry (CTR), (See
   LCD for CTR info) and
I. Patient is monitored for disease progression according to
   established standard of care, and
J. Physician must report the development of metastasis or
   prostate cancer deaths in patients not treated definitively
   who were deemed low risk by the assay.

VIII. Prolaris™ Prostate Cancer Genomic Assay for Men with
      Favorable Intermediate Risk Disease:

      For Medicare members only. Not a covered benefit for
      Centennial and Commercial members.

      For purpose of criteria PHP follows CMS, MolDX: Prolaris™
      Prostate Cancer Genomic Assay for Men with Favorable
      Intermediate Risk Disease LCD (L37226) with related Article
      Policy (A57586). The test help to determine which patients with
      favorable intermediate risk, needle biopsy proven prostate cancer
      (as defined below), can be conservatively managed rather than
      treated with definitive surgery or radiation therapy.

      The Prolaris™ assay is covered for men with favorable
      intermediate risk prostate cancer only when the following clinical
      conditions are met:
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A. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), and

B. Formalin-Fixed, Paraffin-Embedded (FFPE) prostate biopsy specimen with at least 0.5 mm of cancer length, and

C. Patients with favorable intermediate-risk disease, defined by the NCCN as follows:
   a. Predominant Gleason grade 3 (i.e. Gleason score 3+4=7), percentage of positive cores <50%, and no more than 1 NCCN intermediate-risk factor) NCCN intermediate risk factors include T2b-T2c, Gleason score 7, and PSA10-20 ng/mL
   b. Patient has an estimated life expectancy of greater than or equal to 10 years, and
   c. 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
   d. Result will be used to determine treatment between definitive therapy and conservative management, and
   e. Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and
   f. Patient is monitored for disease progression according to established standard of care.

IX. ProMark Risk Score:

For Medicare members only. Not a covered benefit for Centennial and Commercial members.

For purpose of criteria PHP follows CMS MolDX: ProMark Risk Score, LCD (L37011) with related Policy Article (A57587). The test help to determine which patients with early stage, needle biopsy proven prostate cancer can be conservatively managed rather than treated with definitive surgery or radiation therapy.

The ProMark assay is covered only when the following clinical conditions are met:

A. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement), and

B. Patient Stage as defined by one of the following:
   o 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...
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- density of < 0.15 ng/mL/g) OR
  - Low Risk Disease (T1-T2a AND Gleason Score ≤ 6 AND PSA ≤ 10 ng/mL), and

C. Patient has an estimated life expectancy of greater than or equal to 10 years, and

D. Patient is a candidate for and is considering conservative therapy and yet and would be eligible for definitive therapy (radical prostectomy, radiation therapy or brachytherapy), and

E. Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and

F. Test is ordered by a physician certified in the Metamark Genetics Certification and Training Registry (CTR) (See LCD for details on CTR), and

G. Patient is monitored for disease progression according to active surveillance guidelines as recorded in NCCN guidelines, and

H. Physician must report the development of metastasis or prostate cancer deaths in patients not treated definitively who were deemed low risk by the assay.

NON-Covered Test

1. SelectMDx for Prostate Cancer (MDxHealth Inc): Not covered benefit for Medicare, Centennial and Commercial members.

2. ProLaris Biopsy Test; Post-Prostatectomy; Prediction of Prostate Cancer Progression; and Prostate Biopsy. Not covered benefit for Medicare, Centennial and Commercial members.

3. DeCODE Prostate Cancer™ (for assessment of prostate cancer risk or prostate cancer aggressiveness) Not covered benefit for Medicare, Centennial and Commercial members.

4. ConfirmMDX for Prostate Cancer (MDxHealth Inc.) – Not covered benefit for Medicare, Centennial and Commercial members. Insufficient evidence supporting the use of the ConfirmMDX test to help rule-out prostate cancer in repeat biopsy.

Coding

The coding listed in this medical policy is for reference only. Covered and non-covered codes are within this list.
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<table>
<thead>
<tr>
<th>Name of Test</th>
<th>CPT Codes</th>
<th>Test Description of Covered Prostate Cancer Test</th>
</tr>
</thead>
</table>
| Progensa® PCA3 | See below table | Covered for Medicare only  
Progensa® PCA3 Assay |
| BRCA1 & BRCA2 | See below table | Covered for Medicare, Medicaid and Commercial.  
BRCA1 & BRCA2 |
| Decipher® | 81542 | Covered for Medicare only  
Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score  
• For Decipher® Prostate Cancer Classifier Assay or  
• For Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Diseases or  
• For Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Intermediate Risk Disease. |
| Oncotype DX AR-V7 Nucleus Detect | 81479 | Covered for Medicare only  
Unlisted molecular pathology procedure, (For Oncotype DX AR-V7 Nuclear Detect for Men with Castrate Resistant Prostate Cancer (MCRPC)). |
| Oncotype DX® for Low & Intermediate Risk for Prostate Cancer | 0047U | Covered for Medicare, Medicaid & Commercial.  
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.  
• For Genomic Health™ Oncotype DX Prostate Cancer Assay for low risk  
• For Oncotype DX® Genomic Prostate Score for Men with Favorable Intermediate Risk Prostate Cancer |
| ConfirmMDx | 81551 | Covered for Medicare only  
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.  
• For ConfirmMDx Epigenetic molecular Assay. |
| Prolaris™ | 81541 | Covered for Medicare only  
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  
• For Prolaris™ Prostate Cancer Genomic Assay  
• For Prolaris™ Prostate Cancer Genomic Assay for Men with Favorable Intermediate Risk Disease |
| ProMark | 81479 | Covered for Medicare only  
Unlisted molecular pathology procedure (for ProMark Risk Score) |
| 4Kscore | 81539 | Covered for Medicare only  
Oncology (high-grade prostate cancer), biochemical assay of four proteins (Total PSA, Free PSA, Intact PSA, and human kallikrein-2 [hK2]), utilizing plasma or serum, prognostic algorithm reported as a probability score. |
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### CPT Codes

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>81313</td>
<td>PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)</td>
</tr>
<tr>
<td>81321</td>
<td>PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81322</td>
<td>PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant</td>
</tr>
<tr>
<td>81323</td>
<td>PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant</td>
</tr>
<tr>
<td>81479</td>
<td>RB1 (Unlisted molecular pathology procedure)</td>
</tr>
</tbody>
</table>

### ICD-10 Code

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
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<tbody>
<tr>
<td></td>
<td>ICD-10 diagnosis for Progensa® PCA3 Assay, CPT code 81313, 81321, 81322, 81323, 81479.</td>
</tr>
</tbody>
</table>

Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.

- Molecular Diagnostic Tests (MDT), LCD L36807 with related Policy Article (A55202) for covered diagnosis.
- Biomarkers for Oncology, LCD L35396 with related Policy Article (A52986). The PROGENSA® PCA3 Assay (PRED) for covered diagnosis.

## CPT CODEs

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>0102U</td>
<td>Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (17 genes [sequencing and deletion/duplication])</td>
</tr>
<tr>
<td>0103U</td>
<td>Hereditary ovarian cancer (eg, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (24 genes [sequencing and deletion/duplication], EPCAM deletion/duplication only)</td>
</tr>
<tr>
<td>0129U</td>
<td>Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis and deletion/duplication analysis panel (ATM, BRCA1, BRCA2, CDH1, CHEK2, PALB2, PTEN, and TP53)</td>
</tr>
<tr>
<td>0131U</td>
<td>Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (13 genes) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>0132U</td>
<td>Hereditary ovarian cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer),</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>CPT CODEs</th>
<th>CPT codes applicable to BRCA1 and BRCA2 Genetic Testing (L36813/A57771) and (L36715/A56542)</th>
</tr>
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<tbody>
<tr>
<td>0133U</td>
<td>targeted mRNA sequence analysis panel (17 genes) (List separately in addition to code for primary procedure)</td>
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<tr>
<td>0134U</td>
<td>Hereditary prostate cancer-related disorders, targeted mRNA sequence analysis panel (11 genes) (List separately in addition to code for primary procedure)</td>
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<tr>
<td>0135U</td>
<td>Hereditary pan cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (18 genes) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>0136U</td>
<td>Hereditary gynecological cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (12 genes) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>0137U</td>
<td>ATM (ataxia telangiectasia mutated) (eg, ataxia telangiectasia) mRNA sequence analysis (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>0138U</td>
<td>PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) mRNA sequence analysis (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>0157U</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) mRNA sequence analysis (List separately in addition to code for primary procedure)</td>
</tr>
</tbody>
</table>
| 0158U     | APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosus polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure)  
Includes CustomNext + RNA: APC, Ambry Genetics®, Ambry Genetics® |
| 0159U     | MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)  
Includes CustomNext + RNA: MLH1, Ambry Genetics®, Ambry Genetics® |
| 0160U     | MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)  
Includes CustomNext + RNA: MSH2, Ambry Genetics®, Ambry Genetics® |
| 0161U     | MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)  
Includes CustomNext + RNA: MSH6, Ambry Genetics®, Ambry Genetics® |
| 0162U     | PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)  
Includes CustomNext + RNA: Lynch (MLH1, MSH2, MSH6, PMS2), Ambry Genetics®, Ambry Genetics® |

Not every Presbyterian health plan contains the same benefits. Please refer to the member’s specific benefit plan and Schedule of Benefits to determine coverage. [MPMPPC051001]
Genetic Testing for Prostate Cancer
MPM 7.8

<table>
<thead>
<tr>
<th>CPT CODEs</th>
<th>CPT codes applicable to BRCA1 and BRCA2 Genetic Testing (L36813/A57771) and (L36715/A56542)</th>
</tr>
</thead>
<tbody>
<tr>
<td>81162</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)</td>
</tr>
<tr>
<td>81163</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81164</td>
<td>BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)</td>
</tr>
<tr>
<td>81165</td>
<td>BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81166</td>
<td>BRCA1 (BRCA1, DNA repair associated) (EG, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)</td>
</tr>
<tr>
<td>81167</td>
<td>BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)</td>
</tr>
<tr>
<td>81212</td>
<td>BRCA1 (BRCA1, DNA REPAIR ASSOCIATED), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 185DELAG, 5385INSC, 6174DELT variants</td>
</tr>
<tr>
<td>81215</td>
<td>BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant</td>
</tr>
<tr>
<td>81216</td>
<td>BRCA2 (BRCA2, DNA repair associated) (EG, hereditary breast and ovarian cancer) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81217</td>
<td>BRCA2 (BRCA2, DNA repair associated) (EG, hereditary breast and ovarian cancer) gene analysis; known familial variant</td>
</tr>
<tr>
<td>81432</td>
<td>Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, AND TP53</td>
</tr>
<tr>
<td>81433</td>
<td>Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11</td>
</tr>
<tr>
<td>81445</td>
<td>Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (EG, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed</td>
</tr>
<tr>
<td>81455</td>
<td>Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 OR greater genes (EG, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFA, PDGFRB, PGR,</td>
</tr>
</tbody>
</table>
### Genetic Testing for Prostate Cancer
**MPM 7.8**

<table>
<thead>
<tr>
<th>CPT CODEs</th>
<th>Covered diagnosis for Decipher CPT code 81542</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.</td>
</tr>
<tr>
<td></td>
<td>- For MolDX: Decipher® Prostate Cancer Classifier Assay, LCD (L36791), see (<a href="#">A57565</a>) for covered diagnosis.</td>
</tr>
<tr>
<td></td>
<td>- For MolDX: Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Very Low and Low Risk Disease LCD (L37911), see (<a href="#">A57564</a>) for covered diagnosis.</td>
</tr>
<tr>
<td></td>
<td>- Decipher® Biopsy Prostate Cancer Classifier Assay for Men with Intermediate Risk Disease (LCD-L38166), see (<a href="#">A57598</a>) for covered diagnosis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Covered diagnosis for Oncotype DX AR-V7 Nucleus Detect CPT code 81479</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.</td>
</tr>
<tr>
<td></td>
<td>For LCD MolDX: Oncotype DX AR-V7 Nucleus Detect for Men with Metastatic Castrate Resistant Prostate Cancer (MCRPC), LCD (L37915) see (<a href="#">A57582</a>) for covered diagnosis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 CODE</th>
<th>Covered diagnosis for Oncotype DX for Low &amp; Intermediate Risk for Prostate Cancer, CPT code 0047U</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.</td>
</tr>
<tr>
<td></td>
<td>For MolDX: Oncotype DX® Genomic Prostate Score for Men with Favorable Intermediate Risk Prostate Cancer, LCD (L37667), see Article (<a href="#">A56334</a>) for covered diagnosis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 CODE</th>
<th>Covered diagnosis for ConfirmMDX test for CPT 81551</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.</td>
</tr>
<tr>
<td></td>
<td>For MolDX: ConfirmMDx Epigenetic Molecular Assay LCD (L37005), see (<a href="#">A57561</a>) for covered diagnosis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD- 10 CM</th>
<th>Covered diagnosis for Prolaris test, CPT 81541</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.</td>
</tr>
<tr>
<td></td>
<td>- For MolDX Prolaris™ Prostate Cancer Genomic Assay, (LCD-L36787) see (<a href="#">A57585</a>) for covered diagnosis.</td>
</tr>
</tbody>
</table>
Genetic Testing for Prostate Cancer

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<table>
<thead>
<tr>
<th>ICD-10 CM</th>
<th>Covered diagnosis for Prolaris test, CPT 81541</th>
</tr>
</thead>
<tbody>
<tr>
<td>• For MolDX: Prolaris™ Prostate Cancer Genomic Assay for Men with Favorable Intermediate Risk Disease LCD (L37226), see [A57586] for covered diagnosis.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 CM</th>
<th>Covered diagnosis for ProMark Risk Score, CPT 81479- (LCD-L37011/A57587) covered diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.</td>
<td></td>
</tr>
<tr>
<td>For ProMark Risk Score LCD (L37011), see [A57587] for covered diagnosis.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CPT</th>
<th>Covered diagnosis for 4Kscore Test Algorithm, CPT 81539.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refer to the ICD-10 code list in the LCD related Policy Article for applicable diagnosis.</td>
<td></td>
</tr>
<tr>
<td>For 4Kscore Test Algorithm LCD (L37792) see [A56653] for covered diagnosis.</td>
<td></td>
</tr>
</tbody>
</table>

References

1. CMS, Local Coverage Determination, 4Kscore Test Algorithm, Original effective date: 03/21/2019, Revision history date: 12/30/2019, R#2, (LCD-L37792), Cited 07/23/2020, Related Article A56653, revision date: 12/30/2019, R#1 [Cited 07/23/2020]

2. CMS, Local Coverage Article, Local Coverage Determination (LCD): MolDX: Molecular Diagnostic Tests (MDT) (L36807), Revision date: 01/01/202, R13. [Cited 06/12/2020]


4. Hayes, PCA3 Detection Test for Prostate Cancer, Archived June 6, 2018 with C & D2 rating. [Cited 08/27/2019].

5. CMS, Local Coverage Determination, Biomarkers for Oncology (for Progensa) (L35396), Revision date 07/01/2020, R#30. [Cited 07/072020]


7. CMS, Billing and Coding Biomarkers for Oncology (A52986), Revision History date 07/01/2020, R#26. [Cited 07/07/2020].

8. CMS, Wisconsin Physicians Service Ins Corp, MolDX: BRCA1 and BRCA2 Genetic Testing (L36813), Revised 11/01/2019, R7. Related Article (A57771), revision date

Not every Presbyterian health plan contains the same benefits. Please refer to the member’s specific benefit plan and Schedule of Benefits to determine coverage. [MPMPPC051001]
Genetic Testing for Prostate Cancer

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04/02/20, R3. [Cited 06/12/20]


7. CMS, Wisconsin Physician Service Ins. Corp., MolIDX: Decipher® Prostate Cancer Classifier Assay (L36791), revision history date 11/01/2019, R#5 and related Billing and Coding Article (A55398), R1, effective date 01/01/20. [Cited 06/12/2020]


10. Hayes, Decipher Prostate Biopsy (Decipher Biosciences), May 21.2019 with rating D2. [Cited06/12/2020]


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19. NCCN Guidelines, Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 3.2019 **BRCA-Related Breast and/or Ovarian Cancer Syndrome, BRCA1/2 Testing Criteria** (See Pg. 12). [Cited 09/10/2019]


22. Hayes, **SelectMDx** for Prostate Cancer (MDxHealth Inc.), Feb. 23, 2020. Rating D2 [Cited 07/23/2020]

23. NCCN Guidelines Version 2.2019 Prostate Cancer Early Detection (SelectMDx), Biomarker Testing: PSA Derivatives and Other Test, Page MS-23. [Cited 07/12/2019]

24. Hayes, **Prolaris** Biopsy Test (Myriad Genetic Lab), March 28, 2019, (D2 rating), Mar 07, 2020. [Cited 07/23/2020]

25. Hayes, **Prolaris** Post-Prostatectomy (Myriad Genetic Lab), July 9, 2020; (D2 rating). [Cited 07/23/2020]

26. Hayes, **ConfirmMDX** for Prostate Cancer, (MDxHealth Inc), (D2 rating) Jan 10, 2020. [Cited 07/23/2020]

27. Hayes, **Prolaris Biopsy** Test (Myriad Genetic Lab Inc.), March 07, 2020, (D2 rating), Mar 29, 2019. [Cited 07/23/2020]

29. CMS, Local Coverage Determination (LCD): 4Kscore Test Algorithm (L37792), Revision History date: 12/30/2019, R#2. [Cited 07/23/2020]


31. CMS, Local Coverage Determination (LCD): Biomarker Testing (Prior to Initial Biopsy) for Prostate Cancer Diagnosis (L37733), (not in our jurisdiction). Revision History date: 12/01/2019, R#1. Related Article (A56609) [Cited 07/23/2020]


Approval Signatures
Clinical Quality & Utilization Mgmt. Committee: Howard Epstein MD
Medical Directory: Norman White MD

Approval Dates
July 22, 2020

Publications History
05-08-20 Error: Correction of MPM number, from 7.7 to 7.8.
07-22-20 Update policy to add Decipher® Biopsy and 4Kscore for Medicare coverage only.


This Medical Policy is intended to represent clinical guidelines describing medical appropriateness and is developed to assist Presbyterian Health Plan and Presbyterian Insurance Company, Inc. (Presbyterian) Health Services staff and Presbyterian medical directors in

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determination of coverage. The Medical Policy is not a treatment guide and should not be used as such.

For those instances where a member does not meet the criteria described in these guidelines, additional information supporting medical necessity is welcome and may be utilized by the medical director in reviewing the case. Please note that all Presbyterian Medical Policies are available online at: Click here for Medical Policies

1 Includes fallopian tube and primary peritoneal cancers. BRCA – related ovarian cancers are associated with epithelial, non-mucinous histology.
2 NCCN defines blood relative as first- (parents, siblings and children), second- (grandparents, aunts, uncles, nieces and nephews, grandchildren and half-siblings), and third degree-relatives (great-grandparents, great-aunts, great-uncles, great-grandchildren and first cousins) on same side of family.