# Prostate Cancer Genomic Assay
**(Prolaris™)**

**Date of Origin: 02/28/2018** **Last Review Date: 03/28/2018** **Effective Date: 4/1/2018**

**Dates Reviewed:**

**Developed By:** Medical Necessity Criteria Committee

## I. Description

Prolaris™ is an RNA based assay measuring the expression of 31 cell cycle progression (CCP) genes and 15 "housekeeping" genes that act as internal controls and normalization standards in each patient sample. The assay is performed on formalin fixed paraffin-embedded (FFPE) prostate cancer blocks. The assay results are reported as a numerical score along with accompanying interpretive information.

The Prolaris test report that is delivered to the ordering physician includes:

- The patient's Prolaris Score (i.e. cell cycle progression score or "CCP");
- The patient's estimated 10-year prostate cancer mortality risk based on his Prolaris Score in combination with his
- CAPRA score (the combined clinical-cell-cycle risk score, or "CCR");
- A depiction of a threshold for prostate cancer mortality risk below which active surveillance may be safely considered.

The active surveillance threshold was developed based on the CCR score distribution in a training cohort of commercially tested men who might typically be considered for active surveillance according to national cancer guidelines, based on their clinical characteristics alone (n = 505). The training cohort included men meeting the following criteria: Gleason score ≤ 3+4; PSA < 10 ng/ml; <25% positive cores; and T-stage ≤ T2a (N=505). A threshold for the CCR score of 0.8 was conservatively selected such that 90% of the men in the training cohort had scores below the threshold.

The threshold of 0.8 was then validated in two independent cohorts (combined n=765) of conservatively managed men with known outcomes for prostate cancer specific mortality (PCM). The Prolaris Score was a strong prognostic indicator in both validation cohorts, based on previous publications (See references 2 & 3). The threshold was able to dichotomize men into significantly different risk groups. There were no prostate cancer deaths in the group of men with CCR scores below the threshold of 0.8. The CCR score of 0.8 corresponded to a 10-year predicted risk of PCM of about 3%. In summary, the threshold for the CCR score of 0.8 distinguishes men with prostate cancer who may safely pursue active surveillance from those who may not be good candidates.

## II. Criteria: CWQI HCS-0052

A. Prostate cancer genomic assay (Prolaris™) is covered for men with favorable intermediate risk prostate cancer with **ALL** of the following:
    a. Needle biopsy with localized adenocarcinoma of prostate (no clinical evidence of metastasis or lymph node involvement, and
    b. FFPE prostate biopsy specimen with at least 0.5 mm of cancer length, and
    c. Patient Stage defined as ONE of the following:
        i. Very Low Risk Disease as defined by **ALL** of the following:
            1. T1c and
            2. Gleason Score ≤ 6 and
            3. PSA ≤ 1- ng/mL and
            4. Less than 3 prostate cores with tumor and
            5. Less than or equal to 50% cancer in any core and PSA density < 0.15ng/mL)
        ii. Low Risk Disease as defined by **ALL** of the following:
            1. T1-T2a and
            2. Gleason Score ≤ 6 and
            3. PSA ≤ 10 ng/mL
        iii. Favorable Intermediate Risk defined as **ALL** of the following:
            1. Predominant Gleason grade 3 (3+4=7)
            2. Percentage of positive cores < 50%
            3. No more than 1 intermediate risk factor defined as **1 or more** of the following;
                a. T2b-T2c
                b. Gleason score 7
                c. PSA 10-20 ng/mL
    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, and
    g. Patient has not received pelvic radiation or androgen deprivation therapy prior to the biopsy, and
    h. Patient is monitored for disease progression according to established standard of care.

## III. Information Submitted with the Prior Authorization Request:

1. Chart notes
2. Pathology report documenting clinical stage
3. Laboratory reports

## IV. CPT or HCPC codes covered:

| Codes | Description |
|---|---|
| 81541 – New codes as of 1/1/18 | 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 |
| 81479 | Unlisted Molecular Pathology Procedure |

## V. Annual Review History

| Review Date | Revisions | Effective Date |
|---|---|---|
| 03/15/2018 | New Criteria adopted from CMS Noridian LCD for Prolaris Prostate Cancer Genomic Assay (very low, low and intermediate risk) guideline | 6/1/2018 |
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## VI. References


1. Bishoff JT, Freedland SJ, Gerber L, et al. Prognostic utility of the cell cycle progression score generated from biopsy in men treated with prostatectomy. J Urol 2014; 192:409.
2. Cooperberg MR, Simko JP, Cowan JE, et al. Validation of a cell-cycle progression gene panel to improve risk stratification in a contemporary prostatectomy cohort. J Clin Oncol 2013; 31:1428.
3. Cuzick J, Berney DM, Fisher G, et al. Prognostic value of a cell cycle progression signature for prostate cancer death in a conservatively managed needle biopsy cohort. Br J Cancer 2012; 106:1095.
4. Cuzick J, Swanson GP, Fisher G, et al. Prognostic value of an RNA expression signature derived from cell cycle proliferation genes in patients with prostate cancer: a retrospective study. Lancet Oncol 2011; 12:245.
5. Freedland SJ, Gerber L, Reid J, et al. Prognostic utility of cell cycle progression score in men with prostate cancer after primary external beam radiation therapy. Int J Radiat Oncol Biol Phys 2013; 86:848.
6. Cuzick J, Stone S, Fisher G, et al. Validation of an RNA cell cycle progression score for predicting death from prostate cancer in a conservatively managed needle biopsy cohort. Br J Cancer 2015; 113:382.


## Appendix 1 – Applicable Diagnosis Codes:

| Codes | Description |
|---|---|
| C61 | Malignant neoplasm of prostate |
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## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

| Jurisdiction(s): 5, 8 | NCD/LCD Document (s): |
|---|---|
| Noridian Local Coverage Determination (LCD) MolDX-CDD: Prolaris™ Prostrate Cancer Genomic Assay (L36350)<br>Noridian Local Coverage Determination (LCD) MolDX-CDD: Prolaris™ Prostate Cancer Genomic Assay for Men with Favorable Intermediate Risk Disease (L37082) | |
| https://med.noridianmedicare.com/documents/10546/6990983/MolDX-CDD+Prolaris+Prostate+Cancer+Genomic+Assay+LCD/a6555f37-1cea-445d-826b-580c574111a8<br>https://med.noridianmedicare.com/documents/10546/6990983/MolDX+Prolaris+Prostate+Cancer+Genomic+Assay+for+Men+with+Favorable+Intermediate+Risk+Disease | |

| NCD/LCD Document (s): |
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| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| Jurisdiction | Applicable State/US Territory | Contractor |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |