Prostate Cancer Genomic Assay

Date of Origin: 02/28/2018 **Last Review Date: 11/24/2023** **Effective Date: 1/1/2024**

Dates Reviewed: 03/2018, 03/2019, 03/2020, 03/2021, 11/2023

Developed By: Medical Necessity Criteria Committee

I. Description

Prostate cancer is the third most diagnosed cancer worldwide and the second most diagnosed amongst men after lung cancer. Prostate cancer has a strong genetic component. The proportion of prostate cancer attributable to hereditary factors is estimated to be between 5 and 15 %.
Genetic testing to identify pathogenic or likely pathogenic variants in prostate cancer, is valuable in guiding treatment decisions in men with prostate cancer and informing cancer prevention and early detection options for their immediate blood relatives. For example, up to 15% of men with metastatic and 10% of men with localized prostate cancer have mutations in homologous recombination repair (HRR) genes, such as BRCA2, BRCA1, ATM, CHEK2, PALB2, and mismatch repair (MMR) genes (MLH1, MSH2, PMS2, and MSH6).

Several inherited mutations (e.g., BRCA1 and BRCA2) are associated with varying degrees of increased predisposition to prostate cancer. These mutations are linked with a younger age of cancer onset, an aggressive clinical course, and increased cancer mortality. Genetic testing including germline testing of hereditary cancer risk, can inform treatment decisions for men with prostate cancer as well as cancer risk in healthy individuals.

Consensus statements recommend genetic testing (germline/or somatic) for men with metastatic prostate cancer. Germline testing is recommended for men with high- or very high-risk prostate cancer, regardless of family history, for men with a personal history of breast cancer or a positive family history of early onset breast, colorectal, or endometrial cancer (age≤ 50 years); ovarian, exocrine, or pancreatic cancer (any age); prostate cancer 60 years or prostate cancer death; Lynch-syndrome related cancer, especially if diagnosed less 50 years; Ashkenazi Jewish ancestry.

Somatic testing is recommended for men with hormone-sensitive metastatic prostate cancer or castrate-resistant metastatic prostate cancer, particularly for men with personal or family history or Ashkenazi Jewish ancestry and early onset disease.

Test descriptions
The Decipher® prostate cancer assay, a 22-biomarker expression signature using oligonucleotide microarray technology, interrogates 1.4 million RNAs extracted from a formalin-fixed paraffin-embedded (FFPE) tissue block of the index lesion (defined by the highest tumor stage or histological

Gleason grade) from the RP specimen. The biomarkers that comprise the Decipher classifier include cell cycle.

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 test generates a risk score to help predict the likelihood of disease progression in men with localized prostate cancer.

Oncotype DX® Prostate Cancer Assay is prostate biopsy-based 17-gene RT-PCR assay, representing four molecular pathways (androgen signaling, cellular organization, stromal response and proliferation), that provides a biologic measure of cancer aggressiveness. The assay is indicated for men who are considered candidates for active surveillance (AS) (those with NCCN® very low- and low-risk prostate cancer). The assay is designed to inform decisions between AS and immediate treatment.

II. Criteria: CWQI HCS-0225

A. Prostate cancer genomic assay is covered for men with prostate cancer with one or more of the following;
   a. Individuals with NCCN very-low-risk, low-risk, and favorable intermediate-risk prostate cancer who have greater than 10 year life expectancy and who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy; **or**
   b. Individuals with intermediate-risk prostate cancer when deciding whether to add androgen-deprivation therapy to radiation; or
   c. Individuals with an undetectable PSA after prostatectomy for prostate cancer, to determine adjuvant versus salvage radiation therapy or to determine whether to initiate systemic therapies;
   d. Adverse features were identified after radical prostatectomy; or
   e. PSA persistence or recurrence identified during workup for radical prostatectomy

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	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
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score

81479	Unlisted Molecular Pathology Procedure
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

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
03/27/2019	Annual Review: No changes	04/01/2019
03/25/2020	Annual Review: No changes	04/01/2020
03/24/2021	Annual Review: grammar update, no content change	04/01/2021
1/2022	Update: Prostate cancer genomic assay coverage requirements, L38341	
11/22/2023	Annual Review: Criteria updated to allow coverage for Decipher, Oncotype Dx and Prolaris Prostate Cancer genomic Cancer tests. The description and medical necessity requirements were updated as per NCCN guidelines.	01/01/2024

VI. References

1. Ashley Ross, MD, PhDAnthony V D'Amico, MD, PhDStephen Freedland, MD 2022: Molecular prognostic tests for prostate cancer. Retrieved from https://www.uptodate.com/contents/molecular-prognostic-tests-for-prostate-cancer#H3964287674
2. Tuffaha, Edmunfds et al 2023. Guidelines for genetic testing in prostate cancer: a scoping review. Retrieved from https://www.nature.com/articles/s41391-023-00676-0
3. 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.
4. 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.
5. 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.
6. 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.
7. 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.
8. 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.

9. National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Prostate Cancer. https://www.nccn.org/patients/guidelines/content/PDF/prostate-advanced-patient.pdf

Appendix 1 – Applicable Diagnosis Codes:

Codes	Description
C61	Malignant neoplasm of prostate

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):
Local Coverage Determination (LCD) MolDX: Prostate Cancer Genomic Classifier Assay for Men with Localized Disease L38341	
https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=38341&ver=7	

NCD/LCD Document (s):

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