### ProMark Proteomic Prognostic Test

#### Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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#### What are gene expression profiling tests for prostate cancer

**Definition**

Prostate cancer (PC) is the most common cancer and a leading cause of cancer-related deaths worldwide. It is considered a heterogeneous disease with highly variable prognosis.¹

- High-risk prostate cancer (PC) patients treated with radical prostatectomy (RP) undergo risk assessment to assess future disease prognosis and determine optimal treatment strategies. Post-RP pathology findings, such as disease stage, baseline Gleason score, time of biochemical recurrence (BCR) after RP, and PSA doubling-time, are considered strong predictors of disease-associated metastasis and mortality. Following RP, up to 50% of patients have pathology or clinical features that are considered at high risk of recurrence and these patients usually undergo post-RP treatments, including adjuvant or salvage therapy or radiation therapy, which can have serious risks and complications. According to clinical practice guideline recommendations, high-risk patients should undergo 6 to 8 weeks of radiation therapy (RT) following RP. However, approximately 90% of high-risk patients do not develop metastases or die of prostate cancer, and instead may be appropriate candidates for alternative treatment approaches, including active surveillance (AS). As such, many patients may be subjected to unnecessary follow-up procedures and their associated complications, highlighting the need for improved methods of prognostic risk assessment.² ³

- Several genomic biomarkers have been commercially developed to augment the prognostic ability of currently available routine clinical and pathological tests and identify those patients most and least likely to benefit from a specific treatment strategy. Prognostic genomic tests, including gene expression profiling tests, may help to avoid overtreatment by reclassifying those men originally identified as high risk, but who are unlikely to develop metastatic disease. Genomic biomarkers may

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also play a role in assisting clinicians to tailor personalized and more appropriate treatments for subgroups of PC patients, and improve overall health outcomes.\textsuperscript{2,3}

**Test information**

- Gene expression profiles (GEPs) evaluate the expression of several genes using one sample. Gene expression is determined through RNA analysis, using either reverse transcriptase (RT) polymerase chain reaction (PCR) or DNA microarrays.\textsuperscript{4}
- ProMark Proteomic Prognostic Test (Metamark\textsuperscript{®})\textsuperscript{5}
  - According to the manufacturer, ProMark uses an 8-protein signature to predict PC aggressiveness (adverse prostate pathology of Gleason \( \geq 4+3 \) and/or non-organ confined disease [T3a, T3b, N1, or M1]) in patients with biopsy Gleason Scores of 3+3 and 3+4. It is designed to provide a personalized prediction regarding if PC can be managed with or without aggressive forms of treatment.
  - ProMark scores range from 0 to 1, reflecting the probability of adverse pathology at radical prostatectomy.

**Guidelines and evidence**

**National Comprehensive Cancer Network**

- The National Comprehensive Cancer Network (NCCN) 2018 Clinical Practice Guidelines on Prostate Cancer state the following regarding molecular assays:\textsuperscript{6}
  - “Men with low or favorable intermediate risk disease may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, Prolaris, Promark. Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN risk groups.”
  - According to NCCN, the Molecular Diagnostic Services Program (MolDX) recommendations stated the following:\textsuperscript{5}
    - Decipher: “Cover post-RP for 1) pT2 with positive margins; 2) any pT3 disease; 3) rising PSA (above nadir)”
    - Prolaris: “Cover post-biopsy for NCCN very-low, low-risk, and favorable intermediate-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.”
    - Oncotype DX Prostate: “Cover post-biopsy for NCCN very-low, low-risk, and favorable intermediate-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.”
life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy."

- ProMark: “Cover post-biopsy for NCCN very-low and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.”

  - “These molecular biomarker tests have been developed with extensive industry support, guidance, and involvement, and have been marketed under the less rigorous FDA regulatory pathways for biomarkers. Although full assessment of their clinical utility requires prospective randomized clinical trials, which are unlikely to be done, the panel believes that men with low or favorable intermediate disease may consider the use of Decipher, Oncotype DX Prostate, Prolaris, or ProMark during initial risk stratification.”

American Association of Clinical Urologists

The American Association of Clinical Urologists has issued a position statement on genomic testing in prostate cancer that states the following:

- “The AACU supports the use of tissue-based molecular testing as a component of risk stratification in prostate cancer treatment decision making.”

American Urological Association, ASTRO, and the Society of Urologic Oncology

The AUA/ASTRO/SUO guideline for clinically localized prostate cancer states the following:

- “Among most low-risk localized prostate cancer patients, tissue based genomic biomarkers have not shown a clear role in the selection of candidates for active surveillance.”

ProMark

ProMark Literature Review

- One clinical validity study suggests that the ProMark risk score offers additional prognostic information for patients compared with NCCN risk categories alone. However, the current evidence base consists of one clinical validity study and one analytical validity study, both published by the manufacturer. Additional clinical studies are needed to showcase consistency of ProMark test results to accurately predict disease severity following RP. Use of the test in clinical practice will shed light on whether test information is considered sufficient by the medical community to change treatment decision-making and if such changes result in improvement in patient-relevant outcomes, including morbidity and survival.
Criteria

- This test is considered investigational and/or experimental.
  
  - Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.
  
  - In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

References


5. ProMark website. Available at: http://metamarkgenetics.com/healthcare-professionals/our-lab-services/promark

