Oncotype DX for Prostate Cancer

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.

<table>
<thead>
<tr>
<th>Procedures addressed by this guideline</th>
<th>Procedure codes</th>
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<tr>
<td>OncotypeDX Genomic Prostate Score</td>
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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...
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}

- Oncotype DX\textsuperscript{®} Genomic Prostate Score (GPS) (Genomic Health)\textsuperscript{5}
  
  - According to the manufacturer, Oncotype DX prostate cancer assay is a multi-gene expression profiling assay that produces a genomic prostate score (GPS), ranging from 0-100, representing tumor aggressiveness. The Oncotype DX GPS provides risk stratification to properly classify patients. This test is designed to help patients with newly diagnosed, early-stage PC make informed treatment decisions, including active surveillance.
  
  - Oncotype DX GPS uses quantitative RT-PCR for 12 prostate cancer-related genes and 5 control genes (total of 17 genes). It was developed for use with fixed paraffin-embedded (FPE) diagnostic prostate needle biopsies (≥1 mm prostate tumor).

**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{6}
    
    - 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.”
- 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:7

- “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:8

- “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.”

**OncotypeDX Prostate**

**OncotypeDX Prostate Literature Review**9-20

- Oncotype DX may be useful to assist newly diagnosed patients with localized prostate cancer in predicting the probability of adverse pathology and guiding decisions about subsequent treatment interventions or AS. In some studies, Oncotype DX was found to predict adverse prostate cancer pathology beyond currently used clinical parameters and nomograms in patients with very low, low-, and intermediate risk disease. Despite these findings suggesting the potential benefit of Oncotype DX, additional well-designed studies are still needed to adequately determine if the test can allow for clinicians to offer active surveillance safely, thereby minimizing the risk of underestimating the risk of metastasis or local...
tumor spread. In addition, direct evidence of clinical utility of Oncotype DX is lacking. Indirect evidence from clinical studies assessing physician treatment decisions following use of Oncotype DX testing are available; however, it is not clear if any treatment changes resulted in clinically meaningful health outcomes. As such, clinical utility studies in real-world urologic clinical practice are needed to evaluate if treatment practices change with test use, and if these changes result in improved patient-important outcomes, including overall survival and disease-specific survival. Evidence is also lacking regarding how to conduct ongoing monitoring of men who are determined to be low risk with Oncotype DX testing, but high risk with clinical assessment.

Clinical Trials

Engaging Newly Diagnosed Men About Cancer Treatment Options (ENACT)²¹

- “This research is being done to better understand how a new lab test called the Oncotype DX Prostate Cancer Assay may impact what treatment men decide to get and how they feel and think about their choice of treatment.”
- NCT02668276
- Recruiting

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

2. Marrone M, Potosky AL, Penson D, Freedman AN. A 22 Gene-expression Assay, Decipher® (GenomeDx Biosciences) to Predict Five-year Risk of Metastatic


