Decipher Prostate Genomic Classifier

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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.

Procedures addressed by this guideline	Procedure codes
Decipher Prostate Genomic Classifier	81542

Criteria

Decipher Prostate for Radical Prostatectomy (RP)

- No previous gene expression profile testing performed for this diagnosis of cancer, AND
- Member is post-radical prostatectomy, AND
- Post-surgical PSA is undetectable (below 0.2mg/dl), AND
- No evidence of lymph node metastasis identified, AND
- One or more of the following adverse features identified in the surgical specimen:
  - positive surgical margin(s), or
  - extracapsular extension, or
  - seminal vesicle invasion, AND
- Test is being requested to inform adjuvant treatment decisions.

Decipher Prostate for Biopsy

Decipher Prostate for biopsy is not medically necessary.

What are gene expression profiling tests for prostate cancer?

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

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- At the time of diagnosis of localized PC, patients typically undergo a prognostic risk assessment with routine clinical and pathological tests to assess the probability of subsequent progression or metastasis. These prognostic assessments help to identify lower risk patients with indolent disease who may opt for active surveillance (AS), or higher risk patients with more aggressive disease who may benefit from a treatment intervention.
- High-risk prostate cancer (PC) patients treated with radical prostatectomy (RP) also 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 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 either at the time of diagnosis of localized PC or after radical prostatectomy (RP) 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.[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.[4]
- Decipher Prostate Genomic Classifier predicts risk of metastasis to assist with treatment plan and/or intensity.[5]
- "Decipher uses an oligonucleotide microarray to measure the expression of 22 content genes to derive a Decipher score (ranging from 0 to 1.0) and corresponding calibrated probabilities for the following clinical endpoints:"[6,7]

  - "Risk of adverse pathology at RP (i.e., Grade Group 3-5, pT3b-T4, or lymph node involvement)."
  - "5-year and 10-year risk of clinical metastasis and 15-year risk of prostate cancer specific mortality (PCSM) after standard therapy."
- A Decipher score of 0.60 – 1.0 is considered high risk.[5]
- Decipher Prostate for Biopsy
  - “Decipher Prostate Biopsy is intended for use in patients who are diagnosed with localized or regional prostate cancer who have not received pelvic radiation or hormone therapy prior to the biopsy. Decipher results are intended for use as an adjunct to conventional clinical risk factors for determining the metastatic potential of the tumor and patient prognosis.”[6]
- Decipher Prostate for Radical Prostatectomy (RP)
  - "Decipher Prostate RP is intended for use in patients with localized prostate cancer after radical prostatectomy (RP) with undetectable, persistent, or rising prostate-specific antigen (PSA) who are being considered for treatment and have not received pelvic radiation or hormone therapy prior to RP. Decipher results are intended for use as an adjunct to conventional clinical risk factors for determining the metastatic potential of the tumor and patient prognosis.”[7]

Guidelines and evidence

American Association of Clinical Urologists

The American Association of Clinical Urologists (AACU, 2022) has issued a position statement on genomic testing in prostate cancer that states the following:[8]

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

American Society of Clinical Oncology

The American Society of Clinical Oncology (ASCO, 2020) issued a guideline on molecular biomarkers in prostate cancer. This guideline states:[9]

- "Are there molecular biomarkers to diagnose clinically significant prostate cancer?"
  - "Recommendation 2.1. Commercially available molecular biomarkers (ie, Oncotype Dx Prostate [now Genomic Prostate Score], Prolaris, Decipher, and ProMark) may be offered in situations in which the assay result, when considered as a whole with routine clinical factors, is likely to affect management. Routine ordering of molecular biomarkers is not recommended (Type: Evidence based; Evidence quality: Intermediate; Recommendation: Moderate)."
  - "Recommendation 2.2. Any additional molecular biomarkers evaluated do not have sufficient data to be clinically actionable or are not commercially available and

thus should not be offered (Type: Evidence based; Evidence quality: Insufficient; Strength of recommendation: Moderate)."

- "Are there molecular biomarkers to guide the decision of postprostatectomy adjuvant versus salvage radiation?"
  - "Recommendation 3.1. The Expert Panel recommends consideration of a commercially available molecular biomarker (eg, Decipher Genomic Classifier) in situations in which the assay result, when considered as a whole with routine clinical factors, is likely to affect management. In the absence of prospective clinical trial data, routine use of genomic biomarkers in the postprostatectomy setting to determine adjuvant versus salvage radiation or to initiate systemic therapies should not be offered (Type: Evidence based; Evidence quality: Intermediate; Strength of recommendation: Moderate)."
  - "Recommendation 3.2. Any additional molecular biomarkers evaluated do not have sufficient data to be clinically actionable or are not commercially available and thus should not be offered (Type: Evidence based; Evidence quality: Insufficient; Strength of recommendation: Moderate)."

American Urological Association and American Society of Radiation Oncology

The American Urological Association and American Society for Radiation Oncology (AUA/ASTRO, 2022) published an evidence-based guideline on localized prostate cancer endorsed by the Society of Urologic Oncology (SUO) that stated:[10]

- "Clinicians may selectively use tissue-based genomic biomarkers when added risk stratification may alter clinical decision-making. (Expert Opinion)"
- "Clinicians should not routinely use tissue-based genomic biomarkers for risk stratification or clinical decision-making. (Moderate Recommendation; Evidence Level: Grade B)"
- "Regarding tissue-based genomic biomarkers, several currently available commercial tests, including Prolaris, Oncotype Dx [now Genomic Prostate Score], and Decipher, variously offer prediction of adverse pathology as well as the risks of biochemical recurrence, metastasis, and prostate cancer death. However, most of the reported studies to date that evaluated the prognostic ability of these genomic tests did not meet inclusion criteria for the systematic review as the studies used surgical (ie, prostatectomy) rather than biopsy specimens."

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2025) Clinical Practice Guidelines on Prostate Cancer stated the following regarding molecular assays:[11]

- "Retrospective case cohort studies have shown that these assays provide prognostic information independent of NCCN or CAPRA risk groups, which include likelihood of death with conservative management, likelihood of biochemical recurrence after radical prostatectomy or EBRT [external beam radiation therapy], likelihood of

adverse pathologic features after radical prostatectomy, and likelihood of developing metastasis after operation, definitive EBRT, or post-recurrence EBRT."

- "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 and life expectancy greater than or equal to 10 years may consider the use of Decipher, Oncotype DX Prostate [now Genomic Prostate Score], or Prolaris during initial risk stratification. Patients with unfavorable intermediate- and high-risk disease and life expectancy greater than or equal to 10 years may consider the use of Decipher or Prolaris."
- Decipher is included in the Principles of Risk Stratification table as an advanced tool providing prognostic information in individuals with localized prostate cancer or post RP.

With regard to the use of Decipher post-radical prostatectomy (RP), NCCN stated:[11]

- "The panel recommends use of nomograms and consideration of age and comorbidities, clinical and pathologic information, PSA levels, PSADT, and Decipher molecular assays to individualize treatment discussion."
- "The Decipher molecular assay is recommended to inform adjuvant treatment if adverse features are found post-radical prostatectomy, and can be considered as part of counseling for risk stratification in patients with PSA resistance/recurrence after radical prostatectomy (category 2B)."
- "Adverse laboratory/pathologic features include: positive margin(s); seminal vesicle invasion; extracapsular extension; or detectable PSA."

Selected Relevant Publications

The majority of the evidence for Decipher retrospectively evaluates the association between the Decipher score and adverse pathology, biochemical recurrence, or metastasis in men post-RP.[12-37] Low quality evidence suggests Decipher results are associated with metastasis and adverse pathology at initial biopsy. However, these findings are weakened by several limitations, including: overlapping patient populations, retrospective study designs, small sample sizes, and reporting of surrogate outcomes. Several decision impact studies suggest Decipher results may influence clinical decision-making; however, it remains unclear if Decipher-based decision-making ultimately leads to improvements in patient health outcomes. Future trials should prospectively evaluate the impact of Decipher testing on clinical decision-making in large independent cohorts of men and include sufficient follow-up to capture patient-relevant outcomes (e.g., mortality, recurrence, and metastasis). This conclusion is echoed by several systematic reviews.[38-41]

Clinical trials may be ongoing. Additional information can be found at **https://clinicaltrials.gov**.

Note:

This benefit/harm statement only applies to those jurisdictions that do not have Medicare guidance. Based upon the guidelines and evidence provided in the clinical policy, following EviCore's criteria for Decipher Prostate Genomic Classifier will ensure that testing will be available to those members most likely to benefit from the information provided by the assay. For those not meeting criteria, it ensures alternate management strategies are considered. However, it is possible that some members who would benefit from the testing, but do not meet clinical criteria, will not receive an immediate approval for testing.

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