Medical Policy
Gene Expression Analysis for Prostate Cancer Management

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Policy Number: 670
BCBSA Reference Number: 2.04.111

Related Policies
- Gene-Based Tests for Screening, Detection, and/or Management of Prostate Cancer, #333

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Gene expression analysis to guide management of prostate cancer is INVESTIGATIONAL in all situations.

Prior Authorization Information

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CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.
Description
Gene expression profile analysis has been proposed as a means to risk-stratify patients with low-risk prostate cancer, diagnosed by needle biopsy, to guide treatment decisions.

Background
Prostate cancer is the second most common cancer diagnosed among men in the U.S. According to the National Cancer Institute (NCI), nearly 240,000 new cases are expected to be diagnosed in the U.S. in 2013, and associated with around 30,000 deaths. Autopsy studies in the pre-prostate-specific antigen (PSA) screening era have identified incidental cancerous foci in 30% of men 50 years of age, with incidence reaching 75% at age 80 years.(1) However, NCI Surveillance Epidemiology and End Results data show age-adjusted cancer-specific mortality rates for men with prostate cancer have declined from 40 per 100,000 in 1992 to 22 per 100,000 in 2010. This decline has been attributed to a combination of earlier detection via PSA screening and improved therapies.

Localized prostate cancers may appear very similar clinically at diagnosis.(2) However, they often exhibit diverse risk of progression that may not be captured by accepted clinical risk categories (eg, D’Amico criteria) or prognostic tools that are based on clinical findings, including PSA titers, Gleason grade, or tumor stage.(3-7) In studies of conservative management, the risk of localized disease progression based on prostate cancer-specific survival rates at 10 years may range from 15%(8,9) to 20%(10) to perhaps 27% at 20-year follow-up.(11) Among elderly men (70 years or more) with this type of low-risk disease, comorbidities typically supervene as a cause of death; these men will die with prostate cancer present, rather than from the cancer. Other very similar-appearing low-risk tumors may progress unexpectedly rapidly, quickly disseminating and becoming incurable.

The divergent behavior of localized prostate cancers creates uncertainty whether or not to treat immediately.(12,13) A patient may choose definitive treatment upfront.(14) Surgery (radical prostatectomy), external-beam radiation therapy (EBRT), brachytherapy, high-intensity-focused ultrasound, systemic chemotherapy, hormonal therapy, cryosurgery, or combinations are used to treat patients with prostate cancer.(13,15) Complications associated with those treatments most commonly reported (radical prostatectomy, EBRT) and with the greatest variability were incontinence (0-73%) and other genitourinary toxicities (irritative and obstructive symptoms); hematuria (typically 5% or less); gastrointestinal and bowel toxicity, including nausea and loose stools (25-50%); proctopathy, including rectal pain and bleeding (10-39%); and erectile dysfunction, including impotence (50-90%).(15)

American Urological Association (AUA) Guidelines suggest patients with low- and intermediate-risk disease have the option of “active surveillance”, taking into account patient age, patient preferences, and health conditions related to urinary, sexual, and bowel function.(15) With this approach the patient will forgo immediate therapy and continue regular monitoring until signs or symptoms of disease progression are evident, at which point curative treatment is instituted.(16,17)

Given the unpredictable behavior of early prostate cancer, additional prognostic methods to biologically stratify this disease are under investigation. These include microarray-based gene expression profiling, which refers to analysis of mRNA expression levels of many genes simultaneously in a tumor specimen.(18-23) Two microarray-based gene expression profiling tests are now offered, intended to biologically stratify prostate cancers: Prolaris® (Myriad Genetics, Salt Lake City, UT) and Oncotype Dx® Prostate Cancer Assay (Genomic Health, Redwood City, CA). Both use archived tumor specimens as the mRNA source, reverse transcriptase polymerase chain reaction amplification, and the TaqMan low-density array platform (Applied Biosystems, Foster City, CA). Prolaris® is used to quantify expression levels of 31 cell cycle progression (CCP) genes and 15 housekeeper genes to generate a CCP score. Oncotype Dx® Prostate is used to quantify expression levels of 12 cancer-related and 5 reference genes to generate a Genomic Prostate Score (GPS). In the final analysis, the CCP score or GPS are combined in proprietary algorithms with clinical risk criteria (PSA, Gleason grade, tumor stage) to generate new risk
categories (ie, reclassification) intended to reflect biological indolence or aggressiveness of individual lesions, and thus inform management decisions.

Summary
Two gene expression analysis tests—Prolaris® and Oncotype Dx® Prostate—are commercially available. The test results are intended to be used in combination with accepted clinical criteria (Gleason score, prostate-specific antigen [PSA], clinical stage) to stratify biopsy-diagnosed localized prostate cancer according to biological aggressiveness, and direct initial patient management. Direct evidence is insufficient to establish the analytic validity, clinical validity, or clinical utility of either test. Therefore, gene expression analysis for prostate cancer management is considered investigational.

Policy History

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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References