The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Preauthorization is not required but is required if, despite this Protocol position, you feel this service is medically necessary. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

Description

There are a variety of gene-based biomarkers associated with prostate cancer. These tests have the potential to improve the accuracy of risk prediction, diagnosis, staging, or prognosis of prostate cancer.

Background

Prostate cancer is a complex, heterogeneous disease. At the extremes of the spectrum, if left untreated, some prostate cancers behave aggressively, metastasize quickly, and cause mortality, while others are indolent and never progress to cause harm. Current challenges in prostate cancer care are risk assessment; early and accurate detection; monitoring low-risk patients undergoing surveillance only; prediction and detection of recurrence after initial treatment; and assessing efficacy of treatment for advanced disease.

In response to the need for better biomarkers for risk assessment, diagnosis, and prognosis, a variety of exploratory research is ongoing. Some products of this work have already been translated or are in the process of being translated into commercially available tests, including:

- single-nucleotide polymorphisms (SNPs) for risk assessment
- prostate cancer antigen 3 (PCA3) for disease diagnosis and prognosis
- transmembrane serine protease (TMPRSS) fusion genes for diagnosis and prognosis
- multiple gene tests (gene panels) for prostate cancer diagnosis
- gene hypermethylation for diagnosis and prognosis.

Although studies using these tests generate much information that may help elucidate the biologic mechanisms of prostate cancer and eventually help design treatments, the above-mentioned tests are in a developmental phase. Examples are:

- SNP testing as part of genome-scanning tests for prostate cancer risk assessment are offered by a variety of laboratories, such as Navigenics, LabCorp (23andme), and ARUP (deCode), as laboratory-developed tests.
- The PCA3 test is offered in the U.S. by a number of reference laboratories including ARUP, Mayo Medical Laboratories, and LabCorp. Reagents used in testing are developed by Gen-Probe.
- The Prostate Gene Expression Profile was widely announced as available from Clariant, Inc. in January 2009; as of March 2011, the test no longer appears on the listing at the company website.
- Two hypermethylation analyses are currently available or in development:
• LabCorp (Burlington, NC) offers a test for hypermethylated GSTP1 ("Glutathione S-transferase Gene [GSTP1, pi-class] Methylation Assay"), and the required specimen is formalin-fixed, paraffin-embedded tissue. The test is stated to be an adjunct to histopathology.
• MDxHealth (Irvine, CA) offers ConfirmMDx®, a diagnostic test for hypermethylated GSTP1, adenomatous polyposis coli (APC), and RASSF1 (Ras association [RalGDS/AF-6] domain family member 1). The test is marketed as “an epigenetic assay to reduce repeat prostate biopsies,” (1) and the required specimen is formalin-fixed, paraffin-embedded tissue.

**FDA Status**

Only 1 PCA3 test has been submitted to the U.S. Food and Drug Administration (FDA) for premarket approval. The Gen-Probe Progensa® PCA3 Assay was approved by the FDA on February 15, 2012 through the premarket approval process. According to the company’s press release, this assay is “indicated for use in conjunction with other patient information to aid in the decision for repeat biopsy in men 50 years of age or older who have had one or more previous negative prostate biopsies and for whom a repeat biopsy would be recommended by a urologist based on the current standard of care, before consideration of Progensa PCA3 assay results.”

Other tests mentioned in this Protocol, if available, are offered as laboratory-developed tests under the Clinical Laboratory Improvement Amendments (CLIA) licensed laboratories. Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratories offering such tests as a clinical service must meet general regulatory standards of the Clinical Laboratory Improvement Act (CLIA) and must be licensed by CLIA for high-complexity testing.

**Policy (Formerly Corporate Medical Guideline)**

Genetic tests for the screening, detection, and management of prostate cancer are considered investigational. This includes, but is not limited to the following:

- single-nucleotide polymorphisms (SNPs) for risk assessment;
- PCA3 for disease diagnosis and prognosis;
- TMPRSS fusion genes for diagnosis and prognosis;
- multiple gene tests (gene panels) for prostate cancer diagnosis; or
- gene hypermethylation for diagnosis and prognosis.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.
References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


