

Gene Expression Profiling for Prostate Cancer



Medical Coverage Policy

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Change Summary: New policy

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Description

Gene expression profiling (GEP) is a type of laboratory test that measures the activity, or expression, of ribonucleic acid (RNA) of hundreds to thousands of genes at one time to give an overall picture of gene activity. GEP tests are typically performed on tumor tissue but may also be performed on other specimens such as blood. These tests often use microarray technology though other methodologies are also possible. GEP tests are used to determine prognosis, refine risk stratification and/or optimize treatment regimens and have been proposed for prostate cancer. In the setting of prostate cancer, GEP tests may also be referred to as tissue-based molecular assays.

While prostate-specific antigen (PSA) testing is considered the gold standard for prostate cancer screening and management, only biopsy of the prostate gland can establish a prostate cancer diagnosis. However, studies indicate that biopsies fail to

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identify prostate cancer in some men and in certain circumstances, biopsy may be avoidable. To assist with clinical decision making regarding initial or repeat prostate biopsies, laboratory tests such as GEP have been suggested for cancer management. Examples of GEP assays for prostate cancer include, but may not be limited to:

- **ConfirmMDx for Prostate Cancer** is a tumor- (or tissue-) based epigenetic test. An epigenetic test analyzes the tissue next to (or adjacent to) a nearby cancer focus such as prostate cancer. This tissue can contain DNA molecular changes such as methylation. Cancer cells from a biopsy sample may not be detectable; however, methylation changes associated with the cancer may be identified through a technique referred to as methylation-specific polymerase chain reaction (PCR). The ConfirmMDx assay assesses the DNA methylation status of three genes associated with prostate cancer (ie, *GSTP1*, *APC*, *RASSF1*). The assay has been proposed to assist men who may be at high risk for cancer recurrence and are considering a repeat prostate biopsy when the first biopsy result is negative. The test is performed on a formalin-fixed, paraffin-embedded (FFPE) sample. **(Refer to Coverage Limitations section)**
- **Decipher Prostate Biopsy Genomic Classifier** is a tumor- (or tissue-) based test that has been proposed to assist in determining prognosis for individuals diagnosed with prostate cancer with a low-, intermediate- or high-risk biopsy result. This test uses oligonucleotide microarrays to analyze 22 RNA expression biomarkers (ie, *LASP1*, *IQGAP3*, *NFIB*, *S1PR4*, *THBS2*, *AN07*, *PCDH7*, *MYBPC1*, *EPPK1*, *TSBP*, *PBX1*, *NUSAP1*, *ZWILCH*, *UBE2C*, *CAMK2N1*, *RABGAP1*, *PCAT-32*, *GLYATL1P4/PCAT-80*, *TNF RSF19* plus three additional coding and noncoding genomic markers) extracted from a FFPE specimen. **(Refer to Coverage Limitations section)**
- **Decipher Prostate RP Genomic Classifier** is also a tumor-based test that has been suggested to determine prognosis and treatment options for individuals following radical prostatectomy (RP). **(Refer to Coverage Limitations section)**
- **ExoDx Prostate Test** (also known as ExoDx Prostate IntelliScore [EPI]) analyzes RNA in urine by reverse transcriptase quantitative polymerase chain reaction (RT-PCR) and measure expression levels of three genes associated with prostate cancer. The test has been proposed to determine the aggressiveness of prostate

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cancer to assist in determining if prostate biopsy can be avoided. ExoDx may be referred to as a liquid biopsy or GEP test. (**Refer to Coverage Limitations section**)

- **Oncotype DX Genomic Prostate Score (GPS)** is another tumor-based genomic test proposed for use for newly diagnosed prostate cancer to predict high grade disease in men under surveillance or as a prognostic following RP. The test utilizes quantitative reverse transcription polymerase chain reaction (RT-PCR) in which RNA is extracted to measure gene expression from prostate FFPE tissue. The assay analyzes 17 cancer genes (12 genes associated with prostate cancer plus five reference genes). The following genes are included: *AZGP1, FAM13C, KLK2, SRD5A2, FLNC, GSN, GSTM2, TPM2, BGN, COL1A1, SFRPA, TPX2, ARF1, ATP5E, CLTC, GPS1, PGK1*. (**Refer to Coverage Limitations section**)
- **Prolaris Prostate Cancer** (including Prolaris Biopsy Test and Prolaris Post-Prostatectomy Test) is a tumor-based RT-PCR test that evaluates gene expression from FFPE for any individual diagnosed with prostate cancer. A Prolaris Score (also known as cell cycle progression [CCP] score) is then provided and is a measure of cancer aggressiveness. Prolaris evaluates 46 genes (31 cell cycle genes and 15 housekeeping genes). The following genes are included in the analysis: *FOXM1, CDC20, CDKN3, CDC2, KIF11, KIAA0101, NUSAP1, CENPF, ASPM, BUB1B, RRM2, DLGAP5, BIRC5, KIF20A, PLK1, TOP2A, TK1, PBK, ASF1B, C18orf24, RAD54L, PTTG1, CDCA3, MCM10, PRC1, DTL, CEP55, RAD51, CENPM, CDCA8, ORC6L, RPL38, UBA52, PSMC1, RPL4, RPL37, RPS29, SLC25A3, CLTC, TXNL1, PSMA1, RPL8, MMADHC, RPL13A/LOC728658, PPP2CA, MRFAP1*. (**Refer to Coverage Limitations section**)

GEP tests differ from germline genetic tests. Germline genetic testing analyzes an individual's deoxyribonucleic acid (DNA) and can identify genetic variants (mutations) to determine inherited risk of disease. Germline mutations are inherited, are constant throughout an individual's lifetime and identical in all tissue types in the individual. GEP tests evaluate RNA activity in tumor tissue to detect variations that have been acquired over an individual's lifetime. Gene expression is dynamic and responds to cellular environmental signals. Variations are present only in the tissue sampled, are not usually representative of an individual's germline DNA and are not inheritable.

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Coverage Determination

Humana members may **NOT** be eligible under the Plan for **GEP for prostate cancer** including, but may not be limited to:

- ConfirmMDx for Prostate Cancer promoter methylation profiling of three genes (*APC*, *GSTP1*, *RASSF1*) (CPT code 81551)
- Decipher Prostate Biopsy Genomic Classifier mRNA microarray gene expression analysis of 22 genes (CPT code 81542)
- Decipher Prostate RP Genomic Classifier
- ExoDx Prostate Test (also known as ExoDx Prostate IntelliScore [EPI]) GEP by RT-PCR of three genes (*ERG*, *PCA3*, *SPDEF*) using a urine specimen (CPT code 0005U)
- Oncotype DX Genomic Prostate Score gene expression analysis of 17 genes (CPT code 0047U)
- Prolaris Biopsy Test (also referred to as cell-cycle progression score) gene expression analysis of 46 genes (CPT code 81541)
- Prolaris Post-Prostatectomy Test

These are considered experimental/investigational as they are not identified as widely used and generally accepted for the proposed use as reported in nationally recognized peer-reviewed medical literature published in the English language.

Background

Additional information about **prostate cancer** may be found from the following websites:

- [American Cancer Society](#)
- [National Cancer Institute](#)
- [National Library of Medicine](#)

Medical Alternatives

Alternatives to **GEP for prostate cancer** include, but may not be limited to:

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- Management based on traditional clinicopathologic features including, but may not be limited to, life expectancy, PSA level, Gleason score, histologic exam of prostate biopsy

Physician consultation is advised to make an informed decision based on an individual's health needs.

Humana may offer a disease management program for this condition. **The member may call the number on his/her identification card to ask about our programs to help manage his/her care.**

Provider Claims Codes

Any CPT, HCPCS or ICD codes listed on this medical coverage policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81479	Unlisted molecular pathology procedure	Not Covered if used to report GEP for prostate cancer
81541	Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score	Not Covered
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score	Not Covered
81551	Oncology (prostate), promoter methylation profiling by real-time PCR of 3 genes (GSTP1, APC, RASSF1), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a likelihood of prostate cancer detection on repeat biopsy	Not Covered
0005U	Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score	Not Covered

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0047U	Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score	Not Covered
CPT® Category III Code(s)	Description	Comments
No code(s) identified		
HCPCS Code(s)	Description	Comments
No code(s) identified		

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