Gene Expression Profiling for Cancer Indications

Humana

Medicaid Medical Coverage Policy

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Description

Gene expression profiling (GEP) is a 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, such as next generation sequencing (NGS), whole transcriptome sequencing and reverse transcription polymerase chain reaction (RT-PCR) are also used.

GEP tests are currently offered primarily for the management of cancer, most notably breast. Other cancer indications include bladder, colon, cancer of unknown primary (CUP), cutaneous (skin) melanoma, cutaneous squamous cell cancer (SCC), hematologic malignancies, lung cancer, oral cancer, pancreatic cancer, prostate cancer and uveal melanoma.

GEP tests differ from germline genetic tests. GEP tests analyze RNA which is dynamic, responds to cellular environmental signals, are not usually representative of an individual's germline DNA and are not inheritable. Germline genetic testing analyzes an individual's deoxyribonucleic acid (DNA) to detect genetic variants (mutations). Germline mutations are inherited, are constant throughout an individual's lifetime and are identical in every cell of the body.

Coverage Determination

PROSTATE CANCER

ConfirmMDx
Humana members may be eligible under the Plan for **ConfirmMDx (81551)** to manage prostate biopsy results when any of the following indications are met[46]:

- Atypia, suspicious for cancer; **OR**
- Benign but clinical suspicion of cancer persists; **OR**
- High-grade prostatic intraepithelial neoplasia (PIN)

ExoDx Prostate Test or MyProstateScore 2.0
Humana members may be eligible under the Plan for **ExoDx Prostate Test (also known as ExoDx Prostate IntelliScore [EPI]) (0005U) or MyProstateScore 2.0 (MPS2) (0403U)** when the following criteria are met[46]:

- Test performed after repeat PSA and digital rectal exam (DRE), and prior to initial biopsy; **AND**
    - Individual is 45 – 75 years of age with PSA between 3ng/mL and 10 ng/mL and/or very suspicious DRE; **OR**
    - Individual is more than 75 years of age with PSA between 4 ng/mL and 10 ng/mL or very suspicious DRE; **OR**
- Test performed to manage biopsy results when any of the following indications are present:
    - Atypia, suspicious for cancer; **OR**
    - Benign but clinical suspicion of cancer persists; **OR**
    - High-grade prostatic intraepithelial neoplasia (PIN)

UVEAL MELANOMA

DecisionDx-UM
Humana members may be eligible under the Plan for **DecisionDx-UM (81552)** for risk stratification in an individual diagnosed with uveal melanoma.

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for the following **gene expression profiling tests:**

- Cancer of unknown primary (CUP) (also referred to as TOO or tumor of unknown origin) (81540)
- Cxbladder Detect (0012M)
- Cxbladder Monitor (0013M)
- Cxbladder Triage (0363U)

- Cxbladder Triage Plus (0420U)
- Decipher Bladder TURBT (0016M)
- DecisionDx-Melanoma (81529)
- DecisionDx-SCC (0315U)
- DetermaRx (0288U)
- EarlyTect Bladder Cancer Detection (EarlyTect BCD) (0452U)
- Genomic Prostate Score (formerly Oncotype DX Genomic Prostate Score) (0047U)
- myPath Melanoma (0090U)
- Oncotype DX Colon Recurrence Score Test (81525)
- PancreaSeq Genomic Classifier (0313U)
- Pigmented Lesion Assay (0089U)

A review of the current medical literature shows that the **evidence is insufficient** to determine that these services are standard medical treatments. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature (as defined by CMS) examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Humana members may **NOT** be eligible under the Plan for the following **gene expression profiling tests**:

- BBDRisk Dx IHC (0067U)
- CancerDetect (0296U)
- DarwinOncoTarget (formerly known as OncoTarget) and DarwinOncoTreat (formerly known as OncoTreat) (0019U)
- Insight TNBCtype (0153U)
- Lymph2Cx (0017M)
- Lymph3Cx (0120U)
- miR-31now (0069U)
- OncoSignal-7 Pathway (0262U)

A review of the current medical literature shows that there is **no evidence** to determine that these services are standard medical treatments. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature (as defined by CMS) examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Coding Information

Any codes listed on this 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
81504	Oncology (tissue of origin), microarray gene expression profiling of > 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores	
81525	Oncology (colon), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score	
81529	Oncology (cutaneous melanoma), mRNA, gene expression profiling by real-time RT-PCR of 31 genes (28 content and 3 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk, including likelihood of sentinel lymp	
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	
81552	Oncology (uveal melanoma), mRNA, gene expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis	
0005U	Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score	
0012M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm reported as a risk score for having urothelial carcinoma	
0013M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm reported as a risk score for having recurrent urothelial carcinoma	
0016M	Oncology (bladder), mRNA, microarray gene expression profiling of 219 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as molecular subtype (luminal, luminal infiltrated, basal, basal claudin-low, neuroendocrine-like)	

0017M	Oncology (diffuse large B-cell lymphoma [DLBCL]), mRNA, gene expression profiling by fluorescent probe hybridization of 20 genes, formalin-fixed paraffin-embedded tissue, algorithm reported as cell of origin	
0019U	Oncology, RNA, gene expression by whole transcriptome sequencing, formalin-fixed paraffin embedded tissue or fresh frozen tissue, predictive algorithm reported as potential targets for therapeutic agents	
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	
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	
0067U	Oncology (breast), immunohistochemistry, protein expression profiling of 4 biomarkers (matrix metalloproteinase-1 [MMP-1], carcinoembryonic antigen-related cell adhesion molecule 6 [CEACAM6], hyaluronoglucosaminidase [HYAL1], highly expressed in cancer pr	
0069U	Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score	
0089U	Oncology (melanoma), gene expression profiling by RTqPCR, PRAME and LINC00518, superficial collection using adhesive patch(es)	
0090U	Oncology (cutaneous melanoma), mRNA gene expression profiling by RT-PCR of 23 genes (14 content and 9 housekeeping), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a categorical result (ie, benign, intermediate, malignant)	
0120U	Oncology (B-cell lymphoma classification), mRNA, gene expression profiling by fluorescent probe hybridization of 58 genes (45 content and 13 housekeeping genes), formalin-fixed paraffin-embedded tissue, algorithm reported as likelihood for primary mediast	
0153U	Oncology (breast), mRNA, gene expression profiling by next-generation sequencing of 101 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a triple negative breast cancer clinical subtype(s) with information on immune cell inv	

0262U	Oncology (solid tumor), gene expression profiling by real-time RT-PCR of 7 gene pathways (ER, AR, PI3K, MAPK, HH, TGFB, Notch), formalin-fixed paraffin-embedded (FFPE), algorithm reported as gene pathway activity score	
0288U	Oncology (lung), mRNA, quantitative PCR analysis of 11 genes (BAG1, BRCA1, CDC6, CDK2AP1, ERBB3, FUT3, IL11, LCK, RND3, SH3BGR, WNT3A) and 3 reference genes (ESD, TBP, YAP1), formalin-fixed paraffin-embedded (FFPE) tumor tissue, algorithmic interpretation reported as a recurrence risk score	
0296U	Oncology (oral and/or oropharyngeal cancer), gene expression profiling by RNA sequencing at least 20 molecular features (eg, human and/or microbial mRNA), saliva, algorithm reported as positive or negative for signature associated with malignancy	
0313U	Oncology (pancreas), DNA and mRNA next-generation sequencing analysis of 74 genes and analysis of CEA (CEACAM5) gene expression, pancreatic cyst fluid, algorithm reported as a categorical result (ie, negative, low probability of neoplasia or positive, high probability of neoplasia)	
0315U	Oncology (cutaneous squamous cell carcinoma), mRNA gene expression profiling by RT-PCR of 40 genes (34 content and 6 housekeeping), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a categorical risk result (ie, Class 1, Class 2A, Class 2B)	
0363U	Oncology (urothelial), mRNA, gene- expression profiling by realtime quantitative PCR of 5 genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm incorporates age, sex, smoking history, and macrohematuria frequency, reported as a risk score for having urothelial carcinoma	
0403U	Oncology (prostate), mRNA, gene expression profiling of 18 genes, first-catch post-digital rectal examination urine (or processed first-catch urine), algorithm reported as percentage of likelihood of detecting clinically significant prostate cancer	
0420U	Oncology (urothelial), mRNA expression profiling by real-time quantitative PCR of MDK, HOXA13, CDC2, IGFBP5, and CXCR2 in combination with droplet digital PCR (ddPCR) analysis of 6 single-nucleotide polymorphisms (SNPs) genes TERT and FGFR3, urine, algorithm reported as a risk score for urothelial carcinoma	
0452U	Oncology (bladder), methylated PENK DNA detection by linear target enrichment-quantitative methylation-specific real-time PCR (LTE-qMSP), urine, reported as likelihood of bladder cancer	

CPT® Category III Code(s)	Description	Comments
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
S3854	Gene expression profiling panel for use in the management of breast cancer treatment	

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Change Summary

06/03/2025 New Policy.