Gene Expression Profiling for Cancer Indications

Humana

Medical Coverage Policy

Effective Date: 04/27/2023
Revision Date: 04/27/2023
Review Date: 04/27/2023
Policy Number: HUM-0458-058

Change Summary: Updated Title, Description, Coverage Determination, Coverage Limitations, Provider Claims Codes, References

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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 colon, cancer of unknown primary (CUP), cutaneous (skin) melanoma, hematologic malignancies, lung, oral cancer,

squamous cell cancer, urothelial (bladder) and uveal melanoma.

Cancer indications for GEP include, but may not be limited to:

- **Advanced solid tumors** - RNA by whole transcriptome sequencing has been proposed to determine therapeutic options for an individual diagnosed with advanced cancer **(DarwinOncoTarget** [formerly known as OncoTarget] and **DarwinOncoTreat** [formerly known as OncoTreat]). **(Refer to Coverage Limitations section)**

- **Breast cancer** - Proposed for a variety of breast cancer-related indications including, but may not be limited to:

  - Assessment of RNA expression levels of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2). **(Refer to Coverage Limitations section)**

  - Estimate risk of distant recurrence (metastasis) and predict likelihood of benefit from chemotherapy or extended use of endocrine (hormone) therapy for an individual diagnosed with early-stage invasive node negative (no cancer cells detected in lymph glands) or node positive (cancer cells detected in lymph glands) breast cancer. Several tests are commercially available, each analyzing the expression of different numbers of genes and are typically combined with a proprietary algorithm to produce test scores. A low-risk test result may indicate that an individual can safely forgo chemotherapy while a high-risk test score suggests that chemotherapy in addition to endocrine therapy may be necessary. Examples include, but may not be limited to:

    - **Breast Cancer Index (BCI)**
    - **EndoPredict Prognosis Breast Cancer**
    - **MammaPrint**
    - **OncoSignal-7 Pathway (Refer to Coverage Limitations section)**
    - **Oncotype DX Breast Recurrence Score**
    - **Prosigna Breast Cancer Prognostic Gene Signature Assay (PAMS0)**

  - Evaluation of an individual diagnosed with ductal in situ carcinoma (DCIS) to purportedly estimate risk of local recurrence and predict likelihood of benefit from radiation therapy. An example is **Oncotype DX Breast DCIS Score. (Refer to Coverage Limitations section)**

- Molecular subtyping has been proposed to predict response to chemotherapy as well as risk of distant recurrence. Tumors are grouped into distinct categories based on the gene expression pattern of the tumor. Subtypes appear to be associated with different prognoses and responses to treatment options. Examples include, but may not be limited to, **BluePrint** (offered in conjunction with MammaPrint) and **Insight TNBCtype. (Refer to Coverage Limitations section)**

- Predict likelihood of breast cancer for an individual diagnosed with precancerous lesions such as ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), usual ductal hyperplasia (UDH), papilloma and sclerosing adenosis. **BBDRisk Dx** is an example of this type of test. **(Refer to Coverage Limitations section)**

- **Colon cancer** - Proposed as a method to determine risk of relapse for node positive or node negative stage II colon cancer and for metastatic colon cancer to assist in treatment decisions. **Oncotype DX Colon Cancer Recurrence Score Test** is an example of this type of test. **(Refer to Coverage Limitations section)**

- **CUP** (also referred to tumor of unknown origin or tissue of origin [TOO]) - Presented as a way to identify the site of origin for an uncertain cancer diagnosis. **CancerTYPE ID** is an example of this type of test. NeoTYPE Cancer Profile, a molecular profiling test for cancer, is available for use in conjunction with CancerTYPE ID. **(Refer to Coverage Limitations section)**

  For information regarding **NeoTYPE Cancer Profiling,** please refer to Comprehensive Molecular Profiling for Hematologic Malignancies and Solid Tumors Medical Coverage Policy.

- **Cutaneous melanoma** - Several tests have been proposed for the management of melanoma including, but may not be limited to:

  - **DecisionDx-Melanoma** -To aid in determining risk of recurrence or metastasis and likelihood of sentinel lymph node (SLN) positivity in an individual diagnosed with melanoma. **(Refer to Coverage Limitations section)**

- **DecisionDx DiffDx-Melanoma and myPath Melanoma** - To differentiate benign nevi (a birthmark or mole) from malignant melanoma in an individual with melanocytic lesions. **(Refer to Coverage Limitations section)**

- **Merlin Test** - To predict risk of metastasis in an individual with diagnosed with melanoma. **(Refer to Coverage Limitations section)**

- **Pigmented Lesion Assay** - To assist in ruling out melanoma and need for a surgical biopsy for an individual with atypical pigmented lesions. **(Refer to Coverage Limitations section)**

- **Cutaneous SCC** - Under investigation for squamous cell cancer, a type of skin cancer, to identify metastatic risk and assist in treatment decisions **{DecisionDx-SCC). (Refer to Coverage Limitations section)**

- **Hematologic malignancies** - Suggested for classification of hematologic cancers to assist in treatment decisions for leukemia, lymphoma, multiple myeloma, myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPNs). **Lymph2Cx (also referred to as Lymphoma Subtyping Test) and Lymph3Cx** are examples of assays proposed to subclassify lymphoma. **(Refer to Coverage Limitations section)**

- **Lung cancer** - Proposed for use in an individual diagnosed or at risk for lung cancer. Examples include, but may not be limited to:

  - **DetermaRx** has been proposed to determine risk of recurrence and chemotherapy treatment decisions in an individual diagnosed with stage I or stage IIA nonsquamous non-small cell lung cancer (NSCLC). **(Refer to Coverage Limitations section)**

  - **Percepta Bronchial Genomic Sequencing Classifier** to purportedly assess risk and stratify an individual who is a current or former smoker when results of bronchoscopy are indeterminate. **(Refer to Coverage Limitations section)**

  - ***PTEN* gene expression** has been suggested to detect tumor progression for an individual diagnosed with NSCLC. **(Refer to Coverage Limitations section)**

- **Minimal residual disease (MRD)-** Purported to detect MRD, which is a term used for hematologic malignancies and is defined as the small number of cancer cells that remain in the body following treatment. **(Refer to Coverage Limitations Section)**

- **Oropharyngeal/oral cancer** - Proposed for the diagnosis of oral and/or oropharyngeal cancer. **CancerDetect** is an example of this type of testing. **(Refer to Coverage Limitations Section)**

- **Pancreatic cancer** - Suggested as a method to evaluate pancreatic cyst fluid for the early detection of pancreatic cancer. An example is **PancreaSeq Genomic Classifier. (Refer to Coverage Limitations Section)**

- **Tumor mutational burden (TMB)-** Suggested as a methodology to analyze TMB, an emerging biomarker that measures the number of mutations (changes) within the deoxyribonucleic acid (DNA) of cancer cells using tumor biopsy tissue. Determining TMB may be helpful for treatment decisions as well as assessing potential eligibility for clinical trials. **(Refer to Coverage Limitations section)**

- **Urothelial (bladder) cancer** - Proposed for the diagnosis, monitoring and molecular subtyping for urothelial cancer. Examples include, but may not be limited to, **Bladder EpiCheck, Cxbladder Detect, Cxbladder Monitor, Cxbladder Triage, Decipher Bladder Genomic Classifier, Decipher Bladder TURBT, Xpert Bladder Cancer Detection and Xpert Bladder Cancer Monitor. (Refer to Coverage Limitations Section)**

- **Uveal melanoma** - Suggested to predict risk of metastasis for uveal melanoma. Examples include, but may not be limited to, **DecisionDx-PRAME, DecisionDx-UM, DecisionDx-UMSeq. (Refer to Coverage Limitations Section)**

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.

For information regarding **GEP for noncancer indications,** please refer to Gene Expression Profiling for Noncancer Indications Medical Coverage Policy.

For information regarding **GEP for prostate cancer,** please refer to Gene Expression Profiling for Prostate Cancer Medical Coverage Policy.

Coverage Determination

Any state mandates for gene expression profiling take precedence over this medical coverage policy.

Humana members may be eligible under the Plan for **Breast Cancer Index (BCI)** {81518) for an individual diagnosed with breast cancer for the following indications:

- To assess necessity of adjuvant chemotherapy or adjuvant endocrine therapy; **AND**
  - Breast tumor is HER2 negative*; **AND**
  - Breast tumor is hormone receptor (HR) positive; **AND**
  - Breast tumor size greater than 0.5 cm; **AND**
  - Medically eligible for adjuvant therapy (absence of significant comorbidities or is not of advanced age); **AND**
  - Negative axillary lymph nodes (nonmetastatic) (pN0), axillary-node micrometastasis (pNlmi) no greater than 2.0 mm or metastases in 1-3 lymph nodes (pNl); **OR**
- To guide decisions about extended endocrine therapy when the individual to be tested meets the above criteria and has received 5 years of endocrine therapy without recurrence

Humana members may be eligible under the Plan for **EndoPredict Prognosis Breast Cancer** {81522), **MammaPrint** {81521, 81523) or **Oncotype DX Breast Recurrence Score** {81519) for an individual diagnosed with breast cancer and the following criteria are met:

- Breast tumor is HER2 negative*; **AND**
- Breast tumor is HR positive; **AND**
- Breast tumor size greater than 0.5 cm; **AND**
- Medically eligible for adjuvant therapy (absence of significant comorbidities or is not of advanced age); **AND**
- Negative axillary lymph nodes (nonmetastatic) (pN0), axillary-node micrometastasis {pNlmi) no greater than 2.0 mm or metastases in 1-3 lymph nodes {pNl)

Humana members may be eligible under the Plan for **Prosigna Breast Cancer Prognostic Gene Signature Assay** (81520) for an individual diagnosed with breast cancer and the following criteria are met:

- Breast tumor is HER2 negative*; **AND**
- Breast tumor is HR positive; **AND**
- Breast tumor size greater than 0.5 cm; **AND**
- Medically eligible for adjuvant therapy (absence of significant comorbidities or is not of advanced age); **AND**
- Negative axillary lymph nodes (nonmetastatic) (pN0) or axillary-node micrometastasis (pNlmi) no greater than 2.0 mm

Multiple Primary Breast Tumors

Humana members may be eligible under the Plan for **GEP for multiple primary breast tumors** performed with any of the following:

- Breast Cancer Index {BCI) {81518)
- EndoPredict Prognosis Breast Cancer (81522)

- MammaPrint (81521, 81523)
- Oncotype DX Breast Recurrence Score (81519)
- Prosigna Breast Cancer Prognostic Gene Signature Assay (81520)

AND the following criteria are met:

  - Each primary breast tumor must meet the criteria above; **AND**
  - Test result from 1 tumor must be known before testing a subsequent tumor; **AND**
  - Test result from the first tumor indicates a risk classification of low or intermediate

*HER2 status determined by fluorescence in situ hybridization (FISH), immunohistochemistry (IHC) or in situ hybridization (ISH) assay.

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **GEP for any cancer indications** other than those listed above including, but may not be limited to:

- Advanced solid tumor evaluation by RNA gene expression by whole transcriptome sequencing to determine therapeutic options including, but may not be limited to:
  - DarwinOncoTarget (formerly known as OncoTarget) and DarwinOncoTreat (formerly known as OncoTreat) (0019U)
- Assessment of minimal residual disease (MRD)
- Assessment of tumor mutational burden (TMB)
- Breast cancer including, but may not be limited to:
  - Any test other than those listed above including, but may not be limited to:

- BBDRisk Dx IHC (0067U)
- BluePrint
- HER2Dx
- Insight TNBCtype (0153U)
- OncoSignal-7 Pathway (0262U)
- Oncotype DX DCIS Breast Cancer (0045U)

- Determination of ER, PR and HER2 status
- Evaluation of HER2 positive or triple negative breast cancer
- Evaluation of likelihood to benefit from extended endocrine therapy using any test other than Breast Cancer Index (BCI)
- Evaluation of tumors less than or equal to 0.5 cm
- Multiple primary breast tumors if the GEP breast cancer test result on first tumor indicates high risk
- Prosigna for the evaluation of node positive tumors
- Repeat testing on the same breast tumor tissue including with the use of a different GEP test except Breast Cancer Index when used to evaluate likelihood of benefit from extended endocrine therapy and GEP was previously performed to assess necessity of adjuvant therapy
- Use of more than one type of GEP test to assess the same breast lesion except Breast Cancer Index (BCI) when used to evaluate likelihood of benefit from extended endocrine therapy and GEP was previously performed to assess necessity of adjuvant therapy

- Colon cancer including, but may not be limited to, Oncotype DX Colon Recurrence Score Test (81525)
- CUP (also referred to as TOO or tumor of unknown origin) including, but may not be limited to, CancerTYPE ID (81540)
- Cutaneous melanoma including, but may not be limited to:
  - DecisionDx-Melanoma (81529)
  - DecisionDx DiffDx-Melanoma (0314U)
  - Merlin Test
  - myPath Melanoma (0090U)
  - Pigmented Lesion Assay (0089U)
- Cutaneous SCC including, but may not be limited to, DecisionDx-SCC (0315U)
- Hematological malignancies including, but may not be limited to:
  - Acute lymphoblastic (lymphocytic) leukemia (CLL)
  - Acute myelogenous (myeloid) leukemia (AML)
  - B-cell lymphoma classification including, but may not be limited to, Lymph3Cx (0120U)
  - Diffuse large B-cell lymphoma (DCBCL) including, but may not be limited to, Lymph2Cx (also referred to as Lymphoma Subtyping Test) (0017M)
  - Hodgkin lymphoma
  - Multiple myeloma
  - Myelodysplastic syndrome (MOS)
  - Myeloproliferative neoplasm (MPN) (essential thrombocythemia [ET], polycythemia vera [PV] and primary myelofibrosis [PMF]

  - Non-Hodgkin lymphoma
  - Primary mediastinal B-cell lymphoma (PMBCL)

- Lung cancer including, but may not be limited to:
  - DetermaRx (0288U)
  - Percepta Genomic Sequencing Classifier
  - *PTEN* gene expression
- Oral and/or oropharyngeal cancer including, but may not be limited to, CancerDetect(0296U)
- Pancreatic cyst fluid evaluation including, but may not be limited to, PancreaSeq Genomic Classifier (0313U)
- Urothelial cancer including, but may not be limited to:
  - Bladder EpiCheck
  - Cxbladder Detect (0012M)
  - Cxbladder Monitor (0013M)
  - Cxbladder Triage (0363U)
  - Decipher Bladder Genomic Classifier
  - Decipher Bladder TURBT (0016M)
  - Xpert Bladder Cancer Detection
  - Xpert Bladder Cancer Monitor
- Uveal melanoma including, but may not be limited to:
  - DecisionDx-PRAME
  - DecisionDx-UM (81552)
  - DecisionDx-UMSeq

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

Background

Additional information about **cancer, ILD and IPF** may be found from the following websites:

- American Cancer Society
- National Comprehensive Cancer Network
- National Library of Medicine

Medical Alternatives

Alternatives to **GEP for breast and colon cancer** include, but may not be limited to:

- Adjuvant chemotherapy based on evaluation of clinicopathological factors such as patient age, comorbidities, tumor size, tumor grade, numbers of involved lymph nodes, lymphovascular invasion, hormone receptor status and HER2 status

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

- Histopathologic analysis
- Imaging (X-ray, ultrasound, computed tomography [CT] and magnetic resonance imaging [MRI])

Alternatives to **GEP for cutaneous melanoma** include, but may not be limited to:

- Dermoscopy (please refer to Skin Lesion Surveillance Technologies Medical Coverage Policy)
- FISH
- Histopathologic analysis

Alternatives for **GEP for cutaneous SCC** include, but may not be limited to:

- Nodal staging with CT and/or ultrasound
- Histopathologic analysis

Alternatives for **GEP to determine HER2 status** include, but may not be limited to:

- FISH
- IHC
- ISH

Alternatives to **GEP for hematologic malignancies** include, but may not be limited to:

- FISH
- Karyotyping (chromosome analysis)
- NGS for gene fusions and pathogenic mutations

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

- Bronchoscopy
- CT
- Histopathologic analysis
- Positron emission tomography (PET)/CT scan
- Transthoracic needle aspiration

Alternatives to **GEP for precancerous breast lesions** include, but may not be limited to:

- Breast cancer surveillance with clinical breast examinations and mammography
- Endocrine therapy as chemoprevention

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

- CT imaging of abdomen and pelvis
- Cystoscopy

Alternatives to **GEP for uveal melanoma** include, but may not be limited to:

- Fluorescein angiography
- Fundus photography
- Ultrasonography

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
81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2	**Not Covered if used to report any test outlined in Coverage Limitations section**
81479	Unlisted molecular pathology procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
81493	Coronary artery disease, mRNA, gene expression profiling by real-time RT-PCR of 23 genes, utilizing whole peripheral blood, algorithm reported as a risk score	**Not Covered** **Test Obsolete/No Longer Available**
81504	Oncology (tissue of origin), microarray gene expression profiling of> 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores	**Not Covered** **Test Obsolete/No Longer Available**
81518	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy	

81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score	**Not Covered if used to report any test outlined in Coverage Limitations section**
81520	Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes {50 content and 8 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score	
81521	Oncology (breast), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis	
81522	Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes {8 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk score	**Not Covered**
81523	Oncology (breast), mRNA, next-generation sequencing gene expression profiling of 70 content genes and 31 housekeeping genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk to distant metastasis	
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	**Not Covered**
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 lymph node metastasis	**Not Covered**
81540	Oncology (tumor of unknown origin), mRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a probability of a predicted main cancer type and subtype	**Not Covered**

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	**Not Covered**
81599	Unlisted multianalyte assay with algorithmic analysis	**Not Covered if used to report any test outlined in Coverage Limitations section**
84999	Unlisted chemistry procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
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	**Not Covered**
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	**Not Covered**
0016M	Oncology (bladder), mRNA, microarray gene expression profiling of 209 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as molecular subtype (luminal, luminal infiltrated, basal, basal claudin-low, neuroendocrine-like)	**Not Covered**
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	**Not Covered**
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	**Not Covered**

0045U	Oncology (breast ductal carcinoma in situ), 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 recurrence score	**Not Covered**
0067U	Oncology (breast), immunohistochemistry, protein expression profiling of 4 biomarkers (matrix metalloproteinase-1 [MMP-1], carcinoembryonic antigen-related cell adhesion molecule 6 [CEACAM6], hyaluronoglucosaminidase [HYALl], highly expressed in cancer protein [HECl]), formalin-fixed paraffin-embedded precancerous breast tissue, algorithm reported as carcinoma risk score	**Not Covered**
0069U	Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score	**Not Covered** **Test Obsolete/No Longer Available**
0089U	Oncology (melanoma), gene expression profiling by RTqPCR, PRAME and LINC00518, superficial collection using adhesive patch(es)	**Not Covered**
0090U	Oncology (cutaneous melanoma), mRNA gene expression profiling by RT-PCR of 23 genes {14 content and 9 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a categorical result (ie, benign, indeterminate, malignant)	**Not Covered**
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 mediastinal B-cell lymphoma {PMBCL) and diffuse large B-cell lymphoma (DLBCL) with cell of origin subtyping in the latter	**Not Covered**
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 involvement	**Not Covered**

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	**Not Covered**
0288U	Oncology (lung), mRNA, quantitative PCR analysis of 11 genes (BAGI, BRCAI, CDC6, CDK2AP1, ERBB3, FUT3, IIII, LCK, RND3, SH3BGR, WNT3A) and 3 reference genes (ESD, TBP, YAPI), formalin-fixed paraffin-embedded {FFPE) tumor tissue, algorithmic interpretation reported as a recurrence risk score	**Not Covered**
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	**Not Covered**
0313U	Oncology (pancreas), DNA and mRNA next-generation sequencing analysis of 74 genes and analysis of CEA (CEACAMS) gene expression, pancreatic cyst fluid, algorithm reported as a categorical result (ie, negative, low probability of neoplasia or positive, high probability of neoplasia)	**Not Covered**
0314U	Oncology (cutaneous melanoma), mRNA gene expression profiling by RT-PCR of 35 genes {32 content and 3 housekeeping), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a categorical result (ie, benign, intermediate, malignant)	**Not Covered**
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)	**Not Covered**
0363U	Oncology (urothelial), mRNA, gene- expression profiling by real-time quantitative PCR of 5 genes (MDK, HOXA13, CDC2 [CDKI], IGFBPS, and CXCR2), utilizing urine, algorithm incorporates age, sex, smoking history, and macrohematuria frequency, reported as a risk score for having urothelial carcinoma	**Not Covered** **New Code Effective 01/01/2023**

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	**Not Covered if used to report any test outlined in Coverage Limitations section**

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