Genomic and Molecular Biomarker Testing for Cancer

Humana
Medicaid Medical Coverage Policy

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Concurrent (Paired) DNA and RNA Genetic Testing

Description

Concurrent (paired) DNA and RNA genetic testing (also referred to as expanded RNA analysis) is a type of multigene panel test that analyzes DNA in combination with RNA purported to aid with the detection, diagnosis and management of cancer as well as classification of variants of unknown significance (VUS). Paired testing may be offered to an individual who is at increased risk for hereditary cancer, such as colorectal and prostate cancer, and is performed concurrent to DNA testing to identify additional variants (mutations). **+RNAinsight** is an example of paired genetic testing and is conducted as an add-on test for multigene hereditary colorectal cancer panels such as **Lynch syndrome**. +RNAinsight has also been proposed for use with single gene testing for colorectal cancer (eg, *APC*, *MLH1, MSH2, MSH6* and *PMS2*). **+RNAinsight for ProstateNext** has been proposed for individuals diagnosed with prostate cancer.

Coverage Determination

There are no covered indications; refer to Coverage Limitations Section.

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for any of the following tests:

- Concurrent (paired) DNA/RNA genetic testing:
  - +RNAinsight for APC (0157U)
  - +RNAinsight for MSH2 (0159U)
  - +RNAinsight for MSH6 (0160U)
  - +RNAinsight for PMS2 (0161U)
  - +RNAinsight for Lynch Syndrome (0162U)
  - +RNAinsight for ProstateNext (0133U)

A review of the current medical literature shows that the **evidence is insufficient** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service in clinical management.

Coding Information

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CPT® Code(s)	Description	Comments
0133U	Hereditary prostate cancer-related disorders, targeted mRNA sequence analysis panel (11 genes) (List separately in addition to code for primary procedure)	
0157U	APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure)	
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)	
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)	
0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)	
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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HEMATOLOGIC MALIGNANCIES AND SUSPECTED MYELOID DISORDERS
Comprehensive Genomic Profiling/Multigene Panel Testing

Description

Comprehensive genomic profiling (CGP) (also referred to as comprehensive molecular profiling) is a type of test that involves a combination of laboratory methodologies to detect genetic alterations and biomarkers in blood or bone marrow to aid in the management of hematologic malignancies and suspected myeloid disorders. Testing is performed by removing a small sample of tissue for evaluation (eg, bone marrow biopsies, bone marrow aspirates, bone marrow clots), blood draw (peripheral blood samples), or sites located outside of the bone marrow (extramedullary) suspected of harboring a myeloid malignancy. Techniques can vary from test to test and may include but are not limited to, next-generation sequencing (NGS), fluorescence in situ hybridization (FISH) and immunohistochemistry (IHC). Examples of CGP tests include, but are not limited to, **FoundationOne Heme and Neogenomics myeloid and/or heme panels.**

Multigene (or expanded) panels analyze a broad set of genes simultaneously (as opposed to single gene testing that searches for variants in one specific gene). Panels often include medically actionable genes but may also include those with unclear medical management. Targeted (or focused) multigene panels analyze a limited number of genes targeted to a specific condition. An example of a multigene panel includes, but may not be limited to, **MyAML Gene Panel Assay**.

Optical genome mapping (OGM) is a laboratory technique used to analyze long stretches of DNA allowing a broad view of the genome to detect large structural variations. This type of test may be able to detect changes that other assays may miss such as deletions, duplications, insertions, inversions and translocations. OGM has been proposed for use in hematologic malignancies and include tests such as **Augusta Hematology Optical Genome Mapping** and **DH Optical Genome Mapping/Digital Karyotyping Assay.**

Coverage Determination

Comprehensive Genomic Profiling or Multigene Panel Testing for Hematologic Malignancies and Suspected Myeloid Disorders

Humana members may be eligible under the Plan for **comprehensive genomic profiling or multigene panel testing (81450, 81455)** for any of the following indications**:**

- Cancer of the blood and bone marrow (eg, acute myelogenous leukemia [AML])[14]; **OR**
- Myelodysplastic syndrome (MDS)[15]; **OR**
- Myeloproliferative neoplasms (MPNs) which include polycythemia vera (PV), essential thrombocythemia (ET) or primary myelofibrosis (PMF)[16], **OR**
- Suspected myeloid malignancy (does not have a diagnosis of cancer) with undefined cytopenia***** for greater than four months without a known cause[13]; **OR**
- Systemic mastocytosis[18]

MyAML Gene Panel Assay

Humana members may be eligible under the Plan for **MyAML Gene Panel Assay (0050U)** for the management of acute myeloid leukemia (AML)[14].

*****Clinical, laboratory and pathologic assessment are nondiagnostic (such as demonstration of persistent cytopenias [eg, four months] by complete blood count, microscopic examination of a bone marrow biopsy and bone marrow cytogenetic studies. Other than the clinical feature of the number of cytopenias and specific cytogenetic changes found recurrently in myelodysplastic syndrome [MDS], all other diagnostic criteria in MDS rely upon light microscopy findings).[13]

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for **optical genome mapping** including, but not limited to:

- Augusta Hematology Optical Genome Mapping (0331U)
- DH Optical Genome Mapping/Digital Karyotyping Assay (0413U)

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 examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Coding Information

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CPT® Code(s)	Description	Comments
81450	Hematolymphoid neoplasm or disorder, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA	
81455	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis	
0050U	Targeted genomic sequence analysis panel, acute myelogenous leukemia, DNA analysis, 194 genes, interrogation for sequence variants, copy number variants or rearrangements	
0331U	Oncology (hematolymphoid neoplasia), optical genome mapping for copy number alterations and gene rearrangements utilizing DNA from blood or bone marrow, report of clinically significant alterations	
0413U	Oncology (hematolymphoid neoplasm), optical genome mapping for copy number alterations, aneuploidy, and balanced/complex structural rearrangements, DNA from blood or bone marrow, report of clinically significant alterations	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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14. Malcovati L, Galli A, Travaglino E, et al. Clinical significance of somatic mutation in unexplained blood cytopenia. *Blood*. 2017;129(25):3371-3378.

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HEMATOLOGIC MALIGNANCIES AND SUSPECTED MYELOID DISORDERS
Single Gene Testing

Description

Single gene testing may also be performed for hematologic malignancies and suspected myeloid disorders and may be indicated for an individual who exhibits disease symptoms and may be necessary to diagnose or rule out suspected cancer or monitor known cancer. These include, but are not limited to, *ASXL1, BTK, CCND1, CEBPA, EZH2, IDH1, IDH2, MYD88, NPM1, PLCG2, RUNX1, SF3B1, SRSF2, U2AF1, UBA1* and *ZRSR2*.

Coverage Determination

***CEBPA* Gene Testing**
Humana members may be eligible under the Plan for ***CEBPA* gene testing (81218/81219)** for any of the following indications:

- AML (includes APL); **OR**
- MDS; **OR**
- Suspected myeloid malignancy with undefined cytopenia*****

***NPM1* Gene Testing**
Humana members may be eligible under the Plan for ***NPM1* gene testing (81310/0049U)** for any of the following indications:

- AML (includes APL); **OR**
- MDS; **OR**
- Suspected myeloid malignancy with undefined cytopenia*****

***UBA1* Gene Testing**
Humana members may be eligible under the Plan for ***UBA1* gene testing (Q Clamp Plex VEXAS UBA1 Mutation Test [0500U])** when the following criteria are met:

- MDS; **OR**
- VEXAS syndrome; **AND**
    - Individual 18 years of age or older; **AND**
    - Presenting with clinical features of VEXAS syndrome (eg, recurrent fevers, systemic inflammation involving the skin, lung, cartilage and/or vasculature, elevated acute-phase reactants including erythrocyte sedimentation rate [ESR] and ferritin and progressive hematologic abnormalities including cytopenia and dysplastic bone marrow with vacuolization of myeloid and erythroid precursor cells)

*****Clinical, laboratory and pathologic assessment are nondiagnostic (such as demonstration of persistent cytopenias [eg, four months] by complete blood count, microscopic examination of a bone marrow biopsy and bone marrow cytogenetic studies. Other than the clinical feature of the number of cytopenias and specific cytogenetic changes found recurrently in myelodysplastic syndrome [MDS], all other diagnostic criteria in MDS rely upon light microscopy findings).

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

There are no limitations; refer to Coverage Determination Section.

Coding Information

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CPT® Code(s)	Description	Comments
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (eg, acute myeloid leukemia), gene analysis, full gene sequence	
81310	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, exon 12 variants	
0049U	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, quantitative	
0500U	Autoinflammatory disease (VEXAS syndrome), DNA, UBA1 gene mutations, targeted variant analysis (M41T, M41V, M41L, c.118-2A>C, c.118-1G>C, c.118-9_118-2del, S56F, S621C)	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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1. Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization classification of haematolymphoid tumours: myeloid and histiocytic/dendritic neoplasms. *Leukemia*. 2022;36(7):1703-1719.

2. National Comprehensive Cancer Network (NCCN). NCCN Biomarkers Compendium. ASXL1, BTK, CCND1 t(11;14), CEBPA, EZH2, IDH1, IDH2, MYD88, NPM1, PLCG2, RUNX1, SF3B1, SRSF2, U2AF1, ZRSR2. https://nccn.org. Updated 2025.

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15. US Food & Drug Administration (FDA). List of cleared or approved companion diagnostic devices (in vitro and imaging tools). https://fda.gov. Updated March 5, 2025.

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Liquid Biopsy

Description

Liquid biopsy is a minimally invasive laboratory technique that detects cancer-related genetic material, such as circulating tumor DNA (ctDNA) or cell-free DNA (cfDNA), in a blood sample or other body fluids. Unlike traditional tissue biopsies, liquid biopsies can provide a snapshot of tumor activity throughout the body, allowing for earlier detection, real-time monitoring of disease progression and assessment of treatment response. Examples of ctDNA tests include, but are not limited to, **FoundationOne Liquid CDx, Guardant360 CDx** and **LiquidHALLMARK**. Examples of cfDNA tests include, but are not limited to, **RadTox**.

ColonAiQ examines faint tumor signals circulating in an individual's blood that are specific to colon cancer and the precursor polyps of the disease called advanced adenoma. The test uses patented DNA methylation technology that can find small traces of tumor cell-free DNA (cfDNA) in the blood even at incredibly small concentrations.

Colvera is a blood test for the monitoring of colorectal cancer for post-surgical recurrence.

HelioLiver is a blood-based test that combines ctDNA markers and protein biomarkers, analyzed through machine learning to aid in the detection of hepatocellular carcinoma (HCC). The test is intended for use in those at risk for HCC, such as individuals with chronic liver disease or cirrhosis.

LungLB is a laboratory blood-based fluorescence in situ hybridization (FISH) assay for the evaluation of indeterminate pulmonary nodules purposed for the early detection of lung cancer.

Resolution ctDX Lung has been proposed for use in genotyping lung cancer tumors to help determine appropriate treatment options.

SelectMDx is a noninvasive urine-based molecular test that measures the mRNA expression levels of prostate cancer-related genes. It is used to help stratify the risk of high-grade prostate cancer in those with elevated prostate specific antigen (PSA) levels, supporting decisions about proceeding with prostate biopsy.

Coverage Determination

Humana members may be eligible under the Plan for **FoundationOne Liquid CDx (0239U)** when the following criteria are met:

- Individual diagnosed with recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; **AND**

- Tissue-based, comprehensive genomic profiling (CGP) is infeasible (eg, quantity not sufficient for tissue-based CGP or invasive biopsy is medically contraindicated**^**) or specifically in non-small cell lung cancer (NSCLC) tissue-based CGP has shown no actionable mutations

- Individual has decided to seek further cancer treatment (eg, therapeutic chemotherapy)

^Invasive biopsy may be medically contraindicated when the procedure poses significant risk, such as when the only available biopsy site is bone, precarious performance status, significant delay is expected in obtaining tumor tissue for genotyping, when lesions are small or diffuse or when the biopsy site is located in an area that is difficult to access without substantial risk of morbidity.

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for the following liquid biopsy tests:

- Avantect Pancreatic Cancer Test (0410U)
- BTG Early Detection of Pancreatic Cancer (0405U)
- Caris Assure (0485U)
- Colon AIQ (0453U)
- ColoScape (0368U)
- Colvera (0229U)
- DefineMBC (0428U)
- Guardant360 CDx (0242U)
- Guardant Shield (0537U)
- HelioLiver (0333U)
- InVisionFirst-Lung (0388U)
- Liquid HALLMARK (0409U/0530U)
- LungLB (0317U)
- miR Sentinel Prostate Cancer Test (0424U)
- Northstar Response Test (0486U)
- Northstar Select Test (0487U)
- PredicineCARE Assay (0539U)
- RadTox (0285U)
- Resolution ctDx Lung (0179U)
- Select MDx (0339U)

A review of the current medical literature shows that the **evidence is insufficient** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service in clinical management.

Coding Information

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CPT® Code(s)	Description	Comments
81462	Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (eg, plasma), interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants and rearrangements	
81464	Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (eg, plasma), interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants, microsatellite instability, tumor mutation burden, and rearrangements	
0011M	Oncology, prostate cancer, mRNA expression assay of 12 genes (10 content and 2 housekeeping), RT-PCR test utilizing blood plasma and urine, algorithms to predict high-grade prostate cancer risk	
0179U	Oncology (non-small cell lung cancer), cell-free DNA, targeted sequence analysis of 23 genes (single nucleotide variations, insertions and deletions, fusions without prior knowledge of partner/breakpoint, copy number variations), with report of significant mutation(s)	
0229U	BCAT1 (Branched chain amino acid transaminase 1) and IKZF1 (IKAROS family zinc finger 1) (eg, colorectal cancer) promoter methylation analysis	
0239U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free DNA, analysis of 311 or more genes, interrogation for sequence variants, including substitutions, insertions, deletions, select rearrangements, and copy number variations	
0285U	Oncology, response to radiation, cell-free DNA, quantitative branched chain DNA amplification, plasma, reported as a radiation toxicity score	
0242U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 55-74 genes, interrogation for sequence variants, gene copy number amplifications, and gene rearrangements	

0317U	Oncology (lung cancer), four-probe FISH (3q29, 3p22.1, 10q22.3, 10cen) assay, whole blood, predictive algorithm generated evaluation reported as decreased or increased risk for lung cancer	
0326U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 83 or more genes, interrogation for sequence variants, gene copy umber amplifications, gene rearrangements, microsatellite instability and tumor mutational burden	
0333U	Oncology (liver), surveillance for hepatocellular carcinoma (HCC) in high-risk patients, analysis of methylation patterns on circulating cell-free DNA (cfDNA) plus measurement of serum of AFP/AFP-L3 and oncoprotein des-gamma-carboxy-prothrombin (DCP), algorithm reported as normal or abnormal result	
0339U	Oncology (prostate), mRNA expression profiling of HOXC6 and DLX1, reverse transcription polymerase chain reaction (RT-PCR), first-void urine following digital rectal examination, algorithm reported as probability of high-grade cancer	
0368U	Oncology (colorectal cancer), evaluation for mutations of APC, BRAF, CTNNB1, KRAS, NRAS, PIK3CA, SMAD4, and TP53, and methylation markers (MYO1G, KCNQ5, C9ORF50, FLI1, CLIP4, ZNF132 and TWIST1), multiplex quantitative polymerase chain reaction (qPCR), circulating cell-free DNA (cfDNA), plasma, report of risk score for advanced adenoma or colorectal cancer	
0388U	Oncology (non-small cell lung cancer), next-generation sequencing with identification of single nucleotide variants, copy number variants, insertions and deletions, and structural variants in 37 cancer-related genes, plasma, with report for alteration detection	
0405U	Oncology (pancreatic), 59 methylation haplotype block markers, next-generation sequencing, plasma, reported as cancer signal detected or not detected	
0409U	Oncology (solid tumor), DNA (80 genes) and RNA (36 genes), by next-generation sequencing from plasma, including single nucleotide variants, insertions/deletions, copy number alterations, microsatellite instability, and fusions, report showing identified mutations with clinical actionability	
0410U	Oncology (pancreatic), DNA, whole genome sequencing with 5-hydroxymethylcytosine enrichment, whole blood or plasma, algorithm reported as cancer detected or not detected	
0424U	Oncology (prostate), exosome-based analysis of 53 small noncoding RNAs (sncRNAs) by quantitative reverse transcription polymerase chain reaction (RT-qPCR), urine, reported as no	

	molecular evidence, low-, moderate- or elevated-risk of prostate cancer	
0428U	Oncology (breast), targeted hybrid-capture genomic sequence analysis panel, circulating tumor DNA (ctDNA) analysis of 56 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability, and tumor mutation burden	
0453U	Oncology (colorectal cancer), cell-free DNA (cfDNA), methylation-based quantitative PCR assay (SEPTIN9, IKZF1, BCAT1, Septin9-2, VAV3, BCAN), plasma, reported as presence or absence of circulating tumor DNA (ctDNA)	
0485U	Oncology (solid tumor), cell-free DNA and RNA by next-generation sequencing, interpretative report for germline mutations, clonal hematopoiesis of indeterminate potential, and tumor-derived single-nucleotide variants, small insertions/deletions, copy number alterations, fusions, microsatellite instability, and tumor mutational burden	
0486U	Oncology (pan-solid tumor), next-generation sequencing analysis of tumor methylation markers present in cell-free circulating tumor DNA, algorithm reported as quantitative measurement of methylation as a correlate of tumor fraction	
0487U	Oncology (solid tumor), cell-free circulating DNA, targeted genomic sequence analysis panel of 84 genes, interrogation for sequence variants, aneuploidy-corrected gene copy number amplifications and losses, gene rearrangements, and microsatellite instability	
0530U	Oncology (pan-solid tumor), ctDNA, utilizing plasma, next-generation sequencing (NGS) of 77 genes, 8 fusions, microsatellite instability, and tumor mutation burden, interpretative report for single-nucleotide variants, copy-number alterations, with therapy association	
0537U	Oncology (colorectal cancer), analysis of cell-free DNA for epigenomic patterns, next-generation sequencing, >2,500 differentially methylated regions (DMRs), plasma, algorithm reported as positive or negative	
0539U	Oncology (solid tumor), cell-free circulating tumor DNA (ctDNA), 152 genes, next-generation sequencing, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, copy number alterations, and microsatellite instability, using whole-blood samples, mutations with clinical actionability reported as actionable variant	
CPT® Category III Code(s)	**Description**	**Comments**

No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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Minimal Residual Disease

Description

Minimal residual disease (MRD) testing for cancer measures the amount of cancer cells circulating in the blood of an individual with cancer. Although it is a relatively new application of novel genomic technologies, MRD testing has demonstrated its ability to impact cancer diagnosis and treatment thus enabling providers to better assign risk stratification, deploy alternate treatment strategies, or reduce the use of unnecessary adjuvant therapies. Certain MRD tests can be used to monitor the response to immune checkpoint inhibitor (ICI) therapy for individuals with solid tumors. Examples of MRD testing in hematologic malignancies include, but are not limited to, **ClonoSEQ** and **MyMRD**. Examples of MRD testing for solid tumors include, but are not limited to, **Guardant360Response, NavDx** and **Signatera**.

Coverage Determination

HEMATOLOGIC MALIGNANCIES

Humana members may be eligible under the Plan for the assessment of **minimal residual disease (MRD) for hematologic malignancies** using the following tests:

- ClonoSEQ MRD Detection (0364U) for any of the following indications:
    - Acute lymphoblastic leukemia (ALL); **OR**
    - Chronic lymphoblastic leukemia (CLL); **OR**
    - Multiple myeloma; **OR**
- MyMRD Gene Panel Assay (0171U) for acute myeloid leukemia (AML)

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for any of the following MRD tests:

- Genomic Health OncoDetect (81479)
- Guardant360Response (0422U)
- Guardant Reveal (0569U)
- HPV-SEQ (0470U)
- Invitae PCM MRD Monitoring (0307U)
- Invitae PCM Tissue Profiling & MRD Baseline Assay (0306U)
- NavDx (0356U)
- Signatera (0340U)
- UroAmp MRD (0467U)

A review of the current medical literature shows that the **evidence is insufficient** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service 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
0171U	Targeted genomic sequence analysis panel, acute myeloid leukemia, myelodysplastic syndrome, and myeloproliferative neoplasms, DNA analysis, 23 genes, interrogation for sequence variants, rearrangements and minimal residual disease, reported as presence/absence	
0306U	Oncology (minimal residual disease [MRD]), next-generation targeted sequencing analysis, cell-free DNA, initial (baseline) assessment to determine a patient-specific panel for future comparisons to evaluate for MRD	
0307U	Oncology (minimal residual disease [MRD]), next-generation targeted sequencing analysis of a patient-specific panel, cellfree DNA, subsequent assessment with comparison to previously analyzed patient specimens to evaluate for MRD	
0340U	Oncology (pan-cancer), analysis of minimal residual disease (MRD) from plasma, with assays personalized to each patient based on prior next-generation sequencing of the patient's tumor and germline DNA, reported as absence or presence of MRD, with disease-burden correlation, if appropriate	
0356U	Oncology (oropharyngeal or anal), evaluation of 17 DNA biomarkers using droplet digital PCR (ddPCR), cell-free DNA, algorithm reported as a prognostic risk score for cancer recurrence	
0364U	Oncology (hematolymphoid neoplasm), genomic sequence analysis using multiplex (PCR) and next-generation sequencing with algorithm, quantification of dominant clonal sequence(s), reported as presence or absence of minimal residual disease (MRD) with quantitation of disease burden, when appropriate	

0422U	Oncology (pan-solid tumor), analysis of DNA biomarker response to anti-cancer therapy using cell-free circulating DNA, biomarker comparison to a previous baseline pre-treatment cell-free circulating DNA analysis using next-generation sequencing, algorithm reported as a quantitative change from baseline, including specific alterations, if appropriate	
0467U	Oncology (bladder), DNA, next-generation sequencing (NGS) of 60 genes and whole genome aneuploidy, urine, algorithms reported as minimal residual disease (MRD) status positive or negative and quantitative disease burden	
0470U	Oncology (oropharyngeal), detection of minimal residual disease by next-generation sequencing (NGS) based quantitative evaluation of 8 DNA targets, cell-free HPV 16 and 18 DNA from plasma	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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Molecular Markers in Fine Needle Aspirates of Thyroid Nodules

Description

Laboratory examination of cells in thyroid nodules acquired through fine needle aspiration (FNA) has been proposed to assist in exploring the possibility of thyroid cancer. These tests are used to detect molecular markers that are associated with thyroid cancer and are performed when cytopathology cannot determine if the nodule is malignant or benign. This classification is referred to as indeterminate.

Thyroid nodules are abnormal growths or lumps that develop in the thyroid gland. While most are benign, a small percentage are malignant. To determine the likelihood of malignancy, FNA is used to obtain cells from the nodule that is evaluated by cytopathology. FNA results are then assigned to one of 5 categories based on a classification system known as The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). Results categorized as indeterminate warrant further evaluation, which may include repeat FNA, thyroid surgery and/or histopathology. Even with the additional examinations, most cases are ultimately classified as benign. Testing for molecular markers in specimens already attained via FNA potentially eliminates the need for repeat FNA or for surgery.

Thyroid GuidePx is a gene expression profiling test intended for the evaluation of risk for recurrence for an individual with papillary thyroid carcinoma. The test stratifies an individual with papillary thyroid carcinoma into three molecular subgroups and uses a proprietary algorithm to determine risk of recurrence.

ThyroSeq v3 Cancer Risk Classifier (CRC) uses next-generation sequencing (NGS) to analyze the DNA and RNA of over 100 genes in cytologically malignant FNA or resected thyroid tissue to aid in determining risk of recurrence.

Testing for molecular markers in thyroid nodules specimens differs from germline genetic mutation testing. Analysis of molecular markers evaluates specimens for mutations acquired over an individual's lifetime and are present only in the tissue sampled. Germline DNA is constant and identical in all body tissue types and mutations are inheritable.

Coverage Determination

There are no covered indications; refer to Coverage Limitations Section.

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for **molecular markers in thyroid nodule specimens obtained by FNA** for any indications or tests other than those listed above including, but may not be limited to:

- Afirma XA (0204U)
- Evaluation of papillary thyroid carcinoma (eg, Thyroid GuidePx [0362U])
- ThyroSeq v3 Cancer Risk Classifier (CRC) (0287U)
- Use of more than one molecular marker assay

A review of the current medical literature shows that the **evidence is insufficient** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service 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
0018U	Oncology (thyroid), microRNA profiling by RT-PCR of 10 microRNA sequences, utilizing fine needle aspirate, algorithm reported as a positive or negative result for moderate to high risk of malignancy	
0026U	Oncology (thyroid), DNA and mRNA of 112 genes, next-generation sequencing, fine needle aspirate of thyroid nodule, algorithmic analysis reported as a categorical result ("Positive, high probability of malignancy" or "Negative, low probability of malignancy")	
0204U	Oncology (thyroid), mRNA, gene expression analysis of 593 genes (including BRAF, RAS, RET, PAX8, and NTRK) for sequence variants and rearrangements, utilizing fine needle aspirate, reported as detected or not detected	
0245U	Oncology (thyroid), mutation analysis of 10 genes and 37 RNA fusions and expression of 4 mRNA markers using next-generation sequencing, fine needle aspirate, report includes associated risk of malignancy expressed as a percentage	
0287U	Oncology (thyroid), DNA and mRNA, next-generation sequencing analysis of 112 genes, fine needle aspirate or formalin-fixed paraffin-embedded (FFPE) tissue, algorithmic prediction of cancer recurrence, reported as a categorical risk result (low, intermediate, high)	
0362U	Oncology (papillary thyroid cancer), gene-expression profiling via targeted hybrid capture–enrichment RNA sequencing of 82 content genes and 10 housekeeping genes, formalin-fixed	

	paraffin embedded (FFPE) tissue, algorithm reported as one of three molecular subtypes	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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Multianalyte Assays with Algorithmic Analyses

Description

Multianalyte assays with algorithmic analyses (MAAAs) are laboratory measurements that use a mathematic formula to analyze multiple markers that may be associated with a particular disease state and are designed to evaluate disease activity or an individual's risk for disease. The laboratory performs an algorithmic analysis using the results of the assays and sometimes other individual information, such as gender and age and converts the information into a numeric score, which is conveyed on a laboratory report. Generally, MAAAs are exclusive (and/or proprietary) to a single laboratory which owns the algorithm. MAAA testing is used to aid in the diagnosis and evaluation of malignancies such as the following:

- **Bladder Cancer**
  - Bladder CARE is a noninvasive epigenetic urine test intended for the detection of bladder cancer.

- **Lung Cancer**

  - **Nodify CDT test** is intended to detect early-stage lung cancer in an individual who is at moderate to high risk. The test measures the presence of 7 autoantibodies (CAGE, GBU4-5, HuD, MAGE A4, NY-ESO-1, p53 and SOX-2) that are asserted to be involved in early stages of lung cancer development. Results are to be used in conjunction with other clinical data to determine the appropriate diagnostic follow up.

  - **LungOI** is an artificial-intelligence (AI)-based molecular profiling that uses a digitized biopsy image and is proposed for the diagnosis of lung cancer.

  - **VeriStrat** is a serum-based mass spectrometric, eight proteins, including amyloid A, signature proteomic test. It is intended to aid in evaluating prognosis and predicting response to systemic or targeted therapies in an individual with advanced NSCLC.

- **Neuroendocrine Tumors**

  - **NETest** is a multianalyte algorithm, polymerase chain reaction (PCR)-based gene blood test that measures 51 neuroendocrine tumor specific gene transcripts in combination with molecular biomarkers which purportedly allows monitoring of neuroendocrine tumor gene activity levels.

- **Ovarian Cancer**

  - **OvaSuite** is a collection of blood tests (Ova1 Plus [Ova1 and Overa] and OvaWatch) proposed to assess risk of ovarian cancer in an individual diagnosed with an adnexal mass. Proprietary algorithms are applied, along with an individual's features as well as the levels of certain biomarkers. These biomarkers include apolipoprotein A1 (Apo A-1), beta-2 microglobulin (B2M), CA-125, follicle stimulating hormone (FSH), human epididymis protein (HE4), prealbumin and transferrin (TRF). Each test has a specific indication:

  - **Ova1 Plus is comprised of Ova1 and Overa**. Ova1, an FDA-approved test, is performed for an individual with adnexal mass when surgery has been scheduled. If an individual has an intermediate risk result, Overa is automatically reflexed (performed in succession of original test).

  - **Risk of Ovarian Malignancy Algorithm (ROMA)** is an FDA-approved blood test that measures HE4 and CA-125 to evaluate an individual with an adnexal mass to purportedly determine the likelihood of ovarian cancer.

- **Prostate Cancer**

  - **EpiSwitch Prostate Screening Test (PSE)** is a blood test that is used in combination with an individual's PSA score and measures 5 epigenetic biomarkers to determine the likelihood of prostate cancer.

Coverage Determination

There are no covered indications; refer to Coverage Limitations Section.

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for any of the following **MAAAs tests**:

- Bladder CARE Test (0549U)

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 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 any of the following **MAAAs tests**:

- EpiSwitch Prostate Screening Test (PSE) (0433U)
- LungOI (0414U)
- NETest (0007M)
- Nodify CDT (0360U)
- OVA1 (81503)
- ROMA (81500)
- Veristrat (81538)

A review of the current medical literature shows that the **evidence is insufficient** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service 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
81500	Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score	
81503	Oncology (ovarian), biochemical assays of five proteins (CA-125, apolipoprotein A1, beta-2 microglobulin, transferrin, and pre-albumin), utilizing serum, algorithm reported as a risk score	
81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival	
0007M	Oncology (gastrointestinal neuroendocrine tumors), real-time PCR expression analysis of 51 genes, utilizing whole peripheral blood, algorithm reported as a nomogram of tumor disease index	

0021U	Oncology (prostate), detection of 8 autoantibodies (ARF 6, NKX3-1, 5'-UTR-BMI1, CEP 164, 3'-UTR-Ropporin, Desmocollin, AURKAIP-1, CSNK2A2), multiplexed immunoassay and flow cytometry serum, algorithm reported as risk score	
0360U	Oncology (lung), enzyme-linked immunosorbent assay (ELISA) of 7 autoantibodies (p53, NY-ESO-1, CAGE, GBU4-5, SOX2, MAGE A4, and HuD), plasma, algorithm reported as a categorical result for risk of malignancy	
0414U	Oncology (lung), augmentative algorithmic analysis of digitized whole slide imaging for 8 genes (ALK, BRAF, EGFR, ERBB2, MET, NTRK1-3, RET, ROS1), and KRAS G12C and PD-L1, if performed, formalin-fixed paraffin-embedded (FFPE) tissue, reported as positive or negative for each biomarker	
0433U	Oncology (prostate), 5 DNA regulatory markers by quantitative PCR, whole blood, algorithm, including prostate-specific antigen, reported as likelihood of cancer	
0465U	Oncology (urothelial carcinoma), DNA, quantitative methylation-specific PCR of 2 genes (ONECUT2, VIM), algorithmic analysis reported as positive or negative	
0549U	Oncology (urothelial), DNA, quantitative methylated real-time PCR of TRNA-Cys, SIM2, and NKX1-1, using urine, diagnostic algorithm reported as a probability index for bladder cancer and/or upper tract urothelial carcinoma (UTUC)	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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SOLID TUMORS
Comprehensive Genomic Profiling and Multigene Panel Testing

Description

Comprehensive genomic profiling (CGP) (also referred to as comprehensive molecular profiling or tumor profiling) is a laboratory diagnostic method used to analyze the genetic makeup of solid tumors. CGP examines a wide range of genetic variations including mutations, insertions, deletions, amplifications and rearrangements across hundreds of genes. CGP can help guide targeted treatment options. Some CGP tests analyze DNA to detect genetic alterations. These DNA-based tests focus on identifying somatic mutations which occur in tumor cells and are not inherited. Examples include, but are not limited to, **Guardant360 TissueNext, MSK-IMPACT, Oncotype MAP Pan-Cancer Tissue Test and PGDx elio tissue complete**.

Companion diagnostics are laboratory tests that are co-developed with a specific drug to help evaluate if an individual with a specific condition (typically cancer) may benefit from the drug. Companion diagnostics are approved by the US Food & Drug Administration (FDA) typically at the same time as the corresponding pharmacotherapy and can include CGP, molecular biomarker assays as well as single and multigene panel tests. Examples of FDA-approved companion diagnostics include, **MI Cancer Seek, MyChoice CDx,** ~~and~~ **Oncomine Dx Target Test** and **TruSight Oncology Comprehensive Test.**

Cytogenomic neoplasia microarray analysis is a laboratory test that identifies abnormalities in chromosome structure and has been proposed for the diagnosis of cancer. Examples include, but are not limited to, **Clarisure Oligo-SNP and Oncoscan**.

Optical genome mapping, transcriptome, whole exome sequencing (WES) and **whole genome sequencing (WGS)** are other laboratory methods that have been proposed to profile tumors. These techniques purportedly identify genetic variants in an individual's cancer cells to potentially identify actionable genomic mutations to assist with selection of targeted therapies to treat cancer. Examples include, but are not limited to, **EXaCT-1 Whole Exome Sequencing, Praxis Somatic Combined Whole Genome Sequencing and Optimal Genome Mapping, Praxis Somatic Transcriptome** and **Praxis Somatic Whole Genome Sequencing**.

Coverage Determination

Comprehensive Genomic Profiling
Humana members may be eligible under the Plan for **comprehensive genomic profiling for solid tumors (81455)** for any of the following tests when the criteria below are met:

- ExaCT-1 Whole Exome Testing (0036U); **OR**
- Guardant360 Tissue Next (0334U); **OR**
- MSK-IMPACT (0048U); **OR**
- Oncotype MAP PanCancer Tissue Test (0244U); **OR**
- Oncomap ExTra (0329U); **OR**
- PGDx elio tissue complete (0250U);

AND both of the following:

- Individual to be tested has been diagnosed with recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; **AND**

- Individual has decided to seek further cancer treatment (eg, therapeutic chemotherapy)

MI Cancer Seek
Humana members may be eligible under the Plan for MI Cancer Seek (0211U) when the following criteria are met:

- Individual to be tested has been diagnosed with recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; **AND**

- Individual decided to seek further cancer treatment (eg, therapeutic chemotherapy); **AND**
- Individual to be tested for an indication with a corresponding FDA-approved gene or biomarker that establishes eligibility for treatment with a clinically relevant FDA-approved targeted therapy (Table 1)

Table 1
MI Cancer Seek FDA-Approved Indications (The FDA frequently updates the List of Cleared or Approved Companion Diagnostic Devices Website with approvals for companion diagnostics.

Cancer	Indication(s)	Biomarker(s)	FDA-Approved Therapy Under Consideration
Breast Cancer	Metastatic	*PIK3CA*	Alpelisib (Piqray)
Colorectal Cancer	Metastatic	*KRAS* *NRAS*	Panitumumab (Vectibix)
Colorectal Cancer	Metastatic	*BRAF V600E*	Encorafenib (Braftovi) with cetuximab (Erbitux)
Endometrial Carcinoma	Advanced	Not MSI-High	Pembrolizumab (Keytruda) with lenvatinib (Lenvima)
Melanoma	Metastatic or unresectable	*BRAF V600E*	Dabrafenib (Tafinlar)
Melanoma	Metastatic or unresectable	*BRAF V600E*	Vemurafenib (Zelboraf)
Melanoma	Metastatic or unresectable	*BRAF V600E* *BRAF V600K*	Cobimetinib (Cotellic) with vemurafenib (Zelboraf)
Melanoma	Stage III and has undergone lymph node resection, unresectable or stage IV metastatic	*BRAF V600E* *BRAF V600K*	Dabrafenib (Tafinlar) with trametinib (Mekinist)
Melanoma	Unresectable or stage IV metastatic	*BRAF V600E* *BRAF V600K*	Encorafenib (Braftovi) with binimetinib (Mektovi)
Melanoma	Metastatic or unresectable	*BRAF V600E* *BRAF V600K*	Trametinib (Mekinist)
Non-Small Cell Lung Cancer (NSCLC)	Metastatic	*EGFR* exon 19 deletions or exon 21 (L858R) substitution mutations	Afatinib (Gilotrif)
NSCLC	Metastatic	*EGFR* exon 19 deletions or exon 21 (L858R)	Dacomitinib (Vizimpro)

		substitution mutations	
NSCLC	Metastatic	*EGFR* exon 19 deletions or exon 21 (L858R) substitution mutations	Erlotinib (Tarceva)
NSCLC	Metastatic or recurrent	*EGFR* exon 19 deletions or exon 21 (L858R) substitution mutations	Gefitinib (Iressa)
NSCLC	Locally advanced or metastatic	*EGFR* exon 19 deletions or exon 21 (L858R) substitution mutations	Lazertinib (Lazcluze)
NSCLC	Advanced or metastatic	*EGFR* exon 19 deletions or exon 21 (L858R) substitution mutations	Osimertinib (Tagrisso)
Solid Tumors	Metastatic or unresectable	MSI-High	Pembrolizumab (Keytruda)
Solid Tumors	Advanced or recurrent	MSI-High	Dostarlimab-gxly (Jemperli)

MyChoice CDx

Humana members may be eligible under the Plan for **MyChoice CDx (0172U)** when the following criteria are met:

- Epithelial ovarian, fallopian tube or primary peritoneal cancer - advanced; **AND**
- Treatment with olaparib (Lynparza) is under consideration

Oncomine Dx Target Test

Humana members may be eligible under the Plan for **Oncomine Dx Target Test (0022U)** when the following criteria are met:

- Individual to be tested has been diagnosed with recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer[Error! Reference source not found.]; **AND**

- Individual decided to seek further cancer treatment (eg, therapeutic chemotherapy)[Error! Reference source not found.]; **AND**

- Individual to be tested for an indication with a corresponding FDA-approved gene or biomarker that establishes eligibility for treatment with a clinically relevant FDA-approved targeted therapy (Table 2)[121]

Table 2
Oncomine Dx Target Test FDA-Approved Indications (The FDA frequently updates the List of Cleared or Approved Companion Diagnostic Devices Website with approvals for companion diagnostics.

Cancer	Indication(s)	Biomarker(s)	FDA-Approved Therapy Under Consideration
Anaplastic thyroid cancer	Locally advanced or metastatic	*BRAF V600E*	Dabrafenib (Tafinlar) with trametinib (Mekinist)
Astrocytoma	Grade 2	*IDH1* *IDH2*	Vorasidenbi (Voranigo)
Cholangiocarcinoma	Locally advanced or metastatic	*IDH1*	Ivosidenib (Tibsovo)
Medullary thyroid cancer	Advanced or metastatic	*RET*	Selpercatinib (Retevmo)
Non-small cell lung cancer (NSCLC)	Metastatic	*BRAF V600E*	Dabrafenib (Tafinlar) with trametinib (Mekinist)
NSCLC	Metastatic	*EGFR* exon 19 deletion or exon 21 L858R substitution mutation	Gefitinib (Iressa)
NSCLC	Locally advanced or metastatic	*EGFR* exon 20 insertion mutations	Amivantamab-vmjw (Rybrevant)
NSCLC	Unresectable or metastatic	*ERBB2 (HER2)*	Fam-trastuzumab deruxtecan-nxki (Enhertu)
NSCLC	Metastatic	*RET*	Pralsetinib (Gavreto)
NSCLC	Advanced or metastatic	*RET*	Selpercatinib (Retevmo)
NSCLC	Metastatic	*ROS1*	Crizotinib (Xalkori)
Oligodendroglioma	Grade 2	*IDH1* *IDH2*	Vorasidenbi (Voranigo)
Thyroid cancer	Advanced or metastatic	*RET*	Selpercatinib (Retevmo)

TruSight Oncology Comprehensive Test

Humana members may be eligible under the Plan for **TruSight Oncology Comprehensive Test (0543U)** when the following criteria are met:

- Individual to be tested has been diagnosed with recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer[Error! Reference source not found.]; **AND**
- Individual decided to seek further cancer treatment (eg, therapeutic chemotherapy)[Error! Reference source not found.]; **AND**

- Individual to be tested for an indication with a corresponding FDA-approved gene or biomarker that establishes eligibility for treatment with a clinically relevant FDA-approved targeted therapy (Table 3)[121]

Table 3

TruSight Oncology Comprehensive FDA-Approved Indications (The FDA frequently updates the List of Cleared or Approved Companion Diagnostic Devices Website with approvals for companion diagnostics.

Cancer	Indication(s)	Biomarker(s)	FDA-Approved Therapy Under Consideration
Non-small cell lung cancer (NSCLC)	Locally advanced or metastatic	*RET*	Selpercatinib (Retevmo)
Solid tumors	Advanced, metastatic or is not a candidate for surgical resection	*NTRK1* *NTRK2* *NTRK3*	Larotrectinib (Vitrakvi)

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for any of the following tests:

- Praxis Somatic Combined Whole Genome Sequencing and Optical Genome Mapping (0300U)
- Praxis Somatic Optical Genome Mapping Test (0299U)
- Praxis Somatic Transcriptome (0298U)
- Praxis Somatic Whole Genome Sequencing Test (0297U)
- PredicineATLAS Assay (0538U)

A review of the current medical literature shows that the **evidence is insufficient** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service 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
81455	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis	
0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence or absence of variants and associated therapy(ies) to consider	
0036U	Exome (ie, somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal specimen, sequence analyses	
0048U	Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s)	
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score	
0211U	Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association	
0244U	Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single-nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor-mutational burden and microsatellite	

	instability, utilizing formalin-fixed paraffin-embedded tumor tissue	
0250U	Oncology (solid organ neoplasm), targeted genomic sequence DNA analysis of 505 genes, interrogation for somatic alterations (SNVs [single nucleotide variant], small insertions and deletions, one amplification, and four translocations), microsatellite instability and tumor-mutation burden	
0297U	Oncology (pan tumor), whole genome sequencing of paired malignant and normal DNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and variant identification	
0298U	Oncology (pan tumor), whole transcriptome sequencing of paired malignant and normal RNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and expression level and chimeric transcript identification	
0299U	Oncology (pan tumor), whole genome optical genome mapping of paired malignant and normal DNA specimens, fresh frozen tissue, blood, or bone marrow, comparative structural variant identification	
0300U	Oncology (pan tumor), whole genome sequencing and optical genome mapping of paired malignant and normal DNA specimens, fresh tissue, blood, or bone marrow, comparative sequence analyses and variant identification	
0329U	Oncology (neoplasia), exome and transcriptome sequence analysis for sequence variants, gene copy number amplifications and deletions, gene rearrangements, microsatellite instability and tumor mutational burden utilizing DNA and RNA from tumor with DNA from normal blood or saliva for subtraction, report of clinically significant mutation(s) with therapy associations	
0334U	Oncology (solid organ), targeted genomic sequence analysis, formalin-fixed paraffin-embedded (FFPE) tumor tissue, DNA analysis, 84 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden	
0538U	Oncology (solid tumor), next-generation targeted sequencing analysis, formalin-fixed paraffin-embedded (FFPE) tumor tissue, DNA analysis of 600 genes, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, and copy number alterations, microsatellite instability, tumor mutation burden, reported as actionable variant	

0543U	Oncology (solid tumor), next-generation sequencing of DNA from formalin-fixed paraffin-embedded (FFPE) tissue of 517 genes, interrogation for single-nucleotide variants, multi-nucleotide variants, insertions and deletions from DNA, fusions in 24 genes and splice variants in 1 gene from RNA, and tumor mutation burden	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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SOLID TUMORS
Single Gene Testing

Description

Single gene tests analyze only one gene for variants specific to cancer type. Examples of single gene tests include *FGFR, IDH1, IDH2, MGMT, PIK3CA* and *TERT.*

Coverage Determination

***FGFR3* Gene Testing**

Humana members may be eligible under the Plan for ***FGFR3* gene testing (eg, therascreen *FGFR* RGQ RT-PCR Kit [0154U])** for the following indications:

- Bladder cancer – locally advanced, metastatic or unresectable; **AND**
    - To determine eligibility for treatment with erdafitinib (Balversa) or fam-trastuzumab deruxtecan (Enhertu); **OR**
- Salivary gland tumors - metastatic, recurrent, unresectable; **AND**
    - To determine clinical trial eligibility

***IDH1*, *IDH2* and *TERT* Test**

Humana members may be eligible under the Plan for ***IDH1*, *IDH2* and *TERT* Test (0481U)** for the following indications:

- Cholangiocarcinoma - unresectable or metastatic
- Gallbladder cancer - unresectable or metastatic
- Glioma; **OR**
- Melanoma, cutaneous; **OR**
- Uterine carcinoma

***MGMT* Promoter Methylation Testing**

Humana members may be eligible under the Plan for ***MGMT* promoter methylation testing (81287)** for glioma.

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

There are no limitations; refer to Coverage Determination Section.

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
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme) promoter methylation analysis	
0154U	Oncology (urothelial cancer), RNA, analysis by real-time RT-PCR of the FGFR3 (fibroblast growth factor receptor 3) gene analysis (ie, p.R248C [c.742C>T], p.S249C [c.746C>G], p.G370C [c.1108G>T], p.Y373C [c.1118A>G], FGFR3-TACC3v1, and FGFR3-TACC3v3) utilizing formalin-fixed paraffin-embedded urothelial cancer tumor tissue, reported as FGFR gene alteration status	
0155U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A, p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R, p.H1047Y), utilizing formalin-fixed paraffin-embedded breast tumor tissue, reported as PIK3CA gene mutation status	

0177U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha) gene analysis of 11 gene variants utilizing plasma, reported as PIK3CA gene mutation status	
0481U	IDH1 (isocitrate dehydrogenase 1 [NADP+]), IDH2 (isocitrate dehydrogenase 2 [NADP+]), and TERT (telomerase reverse transcriptase) promoter (eg, central nervous system [CNS] tumors), next-generation sequencing (single-nucleotide variants [SNV], deletions, and insertions)	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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Tumor Markers

Description

A **tumor marker** is a protein, antibody, antigen or hormone in the body that may indicate the presence of cancer. Generally, these markers are specific to certain types of cancer and can be detected in blood, body fluids (eg, cerebral spinal fluid [CSF]), stool, tissue and urine samples. The body may produce the marker in response to cancer or the tumor itself may produce the marker. The detection of tumor markers may be used to determine a diagnosis or as an indicator of disease (cancer) progression. It can also be used to document clinical response to treatment. Examples of tumor markers include, but are not limited to:

- **Des-gamma-carboxy prothrombin (DCP)** (also referred to as protein induced by vitamin K absence-II) has been proposed diagnosis and monitoring of hepatocellular carcinoma (liver cancer) as a way to distinguish malignant from benign liver conditions.

- **Human epididymis protein 4 (HE4) (eg, Elecsys HE4 Assay)** has been proposed to aid in the detection and monitoring of ovarian cancer.

- **IsoPSA** is a prostate cancer biomarker test that assesses changes in prostate specific antigen (PSA) proteins to purportedly aid in the detection of high-grade prostate cancer.

Coverage Determination

Human Epididymis Protein 4 (HE4)

Humana members may be eligible under the Plan for **human epididymis protein 4 (HE4) testing (86305)** for the following indications:

- Newly diagnosed ovarian, fallopian tube or primary peritoneal cancer; **OR**

- Suspicious palpable pelvic mass on abdomen/pelvis examination; **AND/OR**

- Ascites, abdominal distention; **AND/OR**

- Symptoms without source of malignancy (eg, bloating, difficulty eating or feeling full quickly, pelvis/ abdomen pain, urinary symptoms [frequency or urgency])

IsoPSA Test

Humana members may be eligible under the Plan for **IsoPSA test (0359U)** when the following criteria are met:

- Individual 50 years of age or older; **AND**
- Prostate specific antigen (PSA) greater than 4 and less than or equal to 25 ng/mL

Coverage Limitations

For members under age 21, requests are reviewed for medical necessity in accordance with Early and Periodic Screening, Diagnostic and Treatment (EPSDT) requirements.

Humana members may **NOT** be eligible under the Plan for **des-gamma-carboxy prothrombin (DCP) (83951) testing**.

A review of the current medical literature shows that the **evidence is insufficient** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service 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
83951	Oncoprotein; des-gamma-carboxy-prothrombin (DCP)	
86305	Human epididymis protein 4 (HE4)	
0359U	Oncology (prostate cancer), analysis of all prostate-specific antigen (PSA) structural isoforms by phase separation and immunoassay, plasma, algorithm reports risk of cancer	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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Change Summary

08/05/2025 New Policy.
01/06/2026 Update, Coverage Change. Provider Claims Codes Update.