Liquid Biopsy

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Medical Coverage Policy

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Related Medical/Pharmacy Coverage Policies

Genetic Testing and Liquid Biopsy for Prostate Cancer

Description

Liquid biopsy is a test usually performed on blood samples, but may be performed on other body fluid samples. It purportedly analyzes the presence of cancer cells released from a tumor that are circulating or fragments of deoxyribonucleic acid (DNA) from tumor cells in the fluid. It may be used to manage treatment, assist in drug selection, determine prognosis as well as therapy response and be used as a minimally invasive alternative to tumor biopsy. The test may have the potential to diagnose cancer at an early stage. Liquid biopsy tests can be US Food & Drug Administration (FDA) approved companion diagnostics (CDx), tests that provide information that is necessary for the safe and effective use of a corresponding drug therapy. The use of a companion diagnostic with a drug is stipulated in the instructions for use in the labeling of both the CDx and the corresponding prescribing drug label (including any generic version). Examples include, but may not be limited to, **Guardant360 CDx**.
Liquid biopsy may identify 2 main biomarkers in an individual with cancer:

- Circulating cell-free DNA (cfDNA), also known as circulating tumor DNA (ctDNA) are DNA fragments from a tumor that circulate in the blood or body fluid of an individual who has cancer. Examples of

cfDNA tests include, but may not be limited to, **GeneStrat, Guardant Tests, LiquidHALLMARK and NavDx. (Refer to Coverage Limitations section)**

- Circulating tumor cells (CTCs) are cancer cells that detach from the primary tumor and travel through the bloodstream or lymphatic system to other parts of the body. Testing purportedly aids in the monitoring of an individual with cancer. **CellSearch** is an example of an FDA-cleared test. **(Refer to Coverage Limitations section)**

Liquid biopsy test may also analyze additional biomarkers such as autoantibodies, cell free ribonucleic acid (RNA) and tumor antigens. These are purported to have the potential to stratify cancer risk or diagnose cancer at an early stage. Examples include, but may not be limited to:

- **Avantect Pancreatic Cancer test** is a blood test that purportedly detects epigenomic and genomic profiles of cfDNA associated with pancreatic cancer. Results indicate whether a cancer signal is detected and treatment recommendations. **(Refer to Coverage Limitations section)**

- **BTG Early Detection of Pancreatic Cancer** is a blood test that analyzes 59 methylation haplotype block markers in plasma using next-generation sequencing, purportedly the results are reported as cancer signal detected or not detected. **(Refer to Coverage Limitations section)**

- **Coloscape Colorectal Cancer Detection test** is a blood test purported to evaluate mutations in 8 genes (*APC, BRAF, CTNNB1, KRAS, NRAS, PIK3CA, SMAD4*, and *TP53*) and 7 methylation markers (C9ORF50, CLIP4, FLI1, KCNQ5, MYO1G, TWIST1 and ZNF132) to report a risk score for advanced adenoma or colorectal cancer (CRC). **(Refer to Coverage Limitations section)**

- **ColonSentry** is a blood test to purportedly stratify an individual's risk for CRC by measuring RNA transcript expression of 6 genes (*ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6*, and *VNN1*) and pairs with the expression level of reference gene IL2RB to create a genetic signature. **(Refer to Coverage Limitations section)**

- **Helioliver** is a blood test purportedly used for surveillance of hepatocellular carcinoma (HCC) in a high-risk individual, by an analysis of methylation patterns on cfDNA combined with measurement of serum of AFP/AFP-L3 and oncoprotein des-gamma-carboxy-prothrombin (DCP), algorithm reported as normal or abnormal result. **(Refer to Coverage Limitations section)**

- **LungLB** is a blood test that uses a predictive algorithm to generate an evaluation reported as a decreased or increased risk for lung cancer. These results are purported to bring certainty into early stage diagnosis confirming for clinicians whether to refer on to biopsy where the low-dose computed tomography (LDCT) scan reveals suspicious nodules. **(Refer to Coverage Limitations section)**

- **OncobiotaLUNG** is a blood test used to measure microbial DNA by NGS, carcinoembryonic antigen and osteopontin by immunoassay. It is purported to detect malignancy risk for lung nodules in early-stage disease. **(Refer to Coverage Limitations section)**

Additional liquid biopsy tests that may aid in predicting an individual's response to therapy include, but may not be limited to:

RadTox is a quantitative DNA amplification test intended for monitoring radiation therapy toxicity in an individual with cancer, enabling providers to monitor side effect severity and tumor response. **(Refer to Coverage Limitations section)**

Coverage Determination

Any state mandates for liquid biopsy take precedence over this medical coverage policy.

Please refer to the member's applicable pharmacy benefit to determine benefit availability and the terms and conditions of coverage for medication for the treatment of cancer.

Humana members may be eligible under the Plan for **liquid biopsy (eg, cfDNA, ctDNA) companion diagnostic testing (CDx)** including, but not limited to, **FoundationOne Liquid CDx (0239U), Guardant360 CDx (0242U) or therascreen PIK3CA RGQ PCR Kit (0177U)** when the following criteria are met:

- Individual diagnosed with recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; **AND**
- Tissue based testing is infeasible (quantity not sufficient or invasive biopsy is medically contraindicated); **AND**
- Individual has not been previously tested for the same genetic content in the primary cancer diagnosis; **AND**
- Individual has decided to seek further cancer treatment (eg, therapeutic chemotherapy); **AND**
- The diagnostic laboratory test must have:
    - FDA approval or clearance as a companion in vitro diagnostic; **AND**
    - FDA approved or cleared indication for use in that individual's cancer; **AND**
    - Results provided to the treating physician for management of the individual using a report template to specify treatment options

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **liquid biopsy (eg, cfDNA, ctDNA, CTC tests [81462, 81463, 81464])** for any indications or tests other than those listed above including, but may not be limited to:

- Avantect Pancreatic Cancer Test (0410U)
- BTG Early Detection of Pancreatic Cancer (0405U)
- CellSearch (86152, 86153)
    - CellSearch Circulating Multiple Myeloma Cell (CMMC) (0337U)
    - CellSearch HER2 Circulating Tumor Cell (CTC-HER2) (0338U)
- CNSide
- ColonSentry
- ColoScape Colorectal Cancer Detection Test (0368U)
- DefineMBC (also known as Epic Sciences ctDNA Metastatic Breast Cancer Panel [0428U])
- FirstSightCRC (0091U)
- Galleri
- GeneStrat
- Guardant tests (eg, Guardant360 [0326U], Guardant360 Response [0422U], Guardant Reveal, Guardant Shield)
- HelioLiver (0333U)
- InVisionFirst LUNG (0388U)
- LiquidHALLMARK (0409U)
- LungLB (0317U)
- NavDx (0356U)
- OncobiotaLUNG (0395U)
- Plasma Focus
- Promoter methylation analysis (BCAT1 or IKZF1) (eg, Colvera [0229U])
- RadTox (0285U)

- Repeat testing or use of more than one liquid biopsy test for the same genetic content (excluding a diagnosis of a new primary cancer made by the treating physician)
- Resolution ctDx Lung (0179U)
- SEPT9 DNA methylation assay (eg, ColoVantage [81327], Epi proColon)
- Signatera (0340U)
- Tempus xF

These are considered experimental/investigational as they have not been 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.

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
81327	SEPT9 (Septin9) (eg, colorectal cancer) promoter methylation analysis	**Not Covered**
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	**Not Covered** **New Code Effective 01/01/2024**
81463	Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (eg, plasma), interrogation for sequence variants; DNA analysis, copy number variants, and microsatellite instability	**Not Covered** **New Code Effective 01/01/2024**
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	**Not Covered** **New Code Effective 01/01/2024**
81479	Unlisted molecular pathology procedure	**Not Covered if used to report any test outlined in this medical coverage policy**

81599	Unlisted multianalyte assay with algorithmic analysis	**Not Covered if used to report any test outlined in this medical coverage policy**
82378	Carcinoembryonic antigen (CEA)	**Not Covered if used to report any test outlined in this medical coverage policy**
86152	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood);	**Not Covered**
86153	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood); physician interpretation and report, when required	**Not Covered**
86304	Immunoassay for tumor antigen, quantitative; CA 125	**Not Covered if used to report any test outlined in this medical coverage policy**
0091U	Oncology (colorectal) screening, cell enumeration of circulating tumor cells, utilizing whole blood, algorithm, for the presence of adenoma or cancer, reported as a positive or negative result	**Not Covered**
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	
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)	**Not Covered**
0229U	BCAT1 (Branched chain amino acid transaminase 1) or IKZF1 (IKAROS family zinc finger 1) (eg, colorectal cancer) promoter methylation analysis	**Not Covered**
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	
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	

0285U	Oncology, response to radiation, cell-free DNA, quantitative branched chain DNA amplification, plasma, reported as a radiation toxicity score	**Not Covered**
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	**Not Covered**
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	**Not Covered**
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	**Not Covered**
0337U	Oncology (plasma cell disorders and myeloma), circulating plasma cell immunologic selection, identification, morphological characterization, and	**Not Covered**
0338U	Oncology (solid tumor), circulating tumor cell selection, identification, morphological characterization, detection and enumeration based on differential EpCAM, cytokeratins 8, 18, and 19, and CD45 protein biomarkers, and quantification of HER2 protein biomarker–expressing cells, peripheral blood	**Not Covered**
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	**Not Covered**
0356U	Oncology (oropharyngeal), evaluation of 17 DNA biomarkers using droplet digital PCR (ddPCR), cell-free DNA, algorithm reported as a prognostic risk score for cancer recurrence	**Not Covered**
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	**Not Covered** **New Code Effective 04/01/2023**

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	**Not Covered** **New Code Effective 07/01/2023**
0395U	Oncology (lung), multi-omics (microbial DNA by shotgun next-generation sequencing and carcinoembryonic antigen and osteopontin by immunoassay), plasma, algorithm reported as malignancy risk for lung nodules in early-stage disease	**Not Covered** **New Code Effective 07/01/2023**
0397U	Oncology (non-small cell lung cancer), cell-free DNA from plasma, targeted sequence analysis of at least 109 genes, including sequence variants, substitutions, insertions, deletions, select rearrangements, and copy number variations	**Not Covered** **Deleted Code Effective 09/30/2023**
0405U	Oncology (pancreatic), 59 methylation haplotype block markers, next-generation sequencing, plasma, reported as cancer signal detected or not detected	**Not Covered** **New Code Effective 10/01/2023**
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	**Not Covered** **New Code Effective 10/01/2023**
0410U	Oncology (pancreatic), DNA, whole genome sequencing with 5-hydroxymethylcytosine enrichment, whole blood or plasma, algorithm reported as cancer detected or not detected	**Not Covered** **New Code Effective 10/01/2023**
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	**Not Covered** **New Code Effective 01/01/2024**
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	**Not Covered** **New Code Effective 01/01/2024**
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

- 01/25/2024 Annual Review, Coverage Change, Updated Coding Information