Liquid Biopsy

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Medicare Advantage Medical Coverage Policy

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Related Medicare Advantage Medical/Pharmacy Coverage Policies

Comprehensive Genomic Profiling and Genetic Testing for Solid Tumors
Genetic Testing for Hematologic Malignancies and Suspected Myeloid Disorders
Measurable (Minimal) Residual Disease Testing

Related CMS Documents

Please refer to CMS Medicare Coverage Database for the most current applicable CMS National Coverage Determination (NCD)/Local Coverage Determination (LCD)/Local Coverage Article (LCA). Refer to CMS website for the most current applicable CMS Online Manual System (IOMs) and Transmittals.

Type	Title	ID Number	Jurisdiction Medicare Administrative Contractors (MACs)	Applicable States/Territories
NCD	Generation Sequencing (NGS)	90.2		

LCD LCA	Billing and Coding: MolDx: SEPT9 Gene Test Billing and Coding: MolDX: Testing of Multiple Genes MolDX: Defining panel services in MolDX MolDX: Inivata™, InvisionFirst®, Liquid Biopsy for Patients with Lung Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Phenotypic Biomarker Detection in Circulating Tumor Cells MolDX: Plasma-Based Genomic Profiling in Solid Tumors	A55206 A57880 A59700 L37921 A56333 L36807 A57772 L38678 A58205 L38168 A57936	J5 - Wisconsin Physicians Service Insurance Corporation J8 - Wisconsin Physicians Service Insurance Corporation	IA, KS, MO, NE IN, MI
LCD	Billing and Coding: Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms Molecular Pathology Procedures	A56867 L35000	J6 - National Government Services, Inc. JK - National Government Services, Inc.	IL, MN, WI CT, NY, ME, MA, NH, RI, VT
LCD LCA	Billing and Coding: MolDx: SEPT9 Gene Test Billing and Coding: MolDX: Testing of Multiple Genes MolDX: Defining panel services in MolDX MolDX: Inivata™, InvisionFirst®, Liquid Biopsy for Patients with Lung Cancer	A54300 A57910 A59698 L37903 A56982 L36021	J15 - CGS Administrators, LLC	KY, OH

	MolDX: Molecular Diagnostic Tests (MDT) MolDX: Phenotypic Biomarker Detection in Circulating Tumor Cells MolDX: Plasma-Based Genomic Profiling in Solid Tumors	A56973 L38584 A58063 L38065 A57917		
LCD LCA	Billing and Coding: Guardant360® Billing and Coding: MolDX: SEPT9 Gene Test Billing and Coding: MolDX: Testing of Multiple Genes MolDX: Defining panel services in MolDX MolDX: Inivata™, InvisionFirst®, Liquid Biopsy for Patients with Lung Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Phenotypic Biomarker Detection in Circulating Tumor Cells MolDX: Plasma-Based Genomic Profiling in Solid Tumors	A58192 A55623 A58120 A59685 L37897 A57664 L35160 A57526 L38643 A58183 L39230 A58973	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
LCD LCA	Billing and Coding: Guardant360® Billing and Coding: MolDX: SEPT9 Gene Test Billing and Coding: MolDX: Testing of Multiple Genes	A58214 A55628 A58121 A59687	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY

	MolDX: Defining panel services in MolDX MolDX: Inivata™, InvisionFirst®, Liquid Biopsy for Patients with Lung Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Phenotypic Biomarker Detection in Circulating Tumor Cells MolDX: Plasma-Based Genomic Profiling in Solid Tumors	L37899 A57665 L36256 A57527 L38645 A58185 L39232 A58975		
LCD LCA	Billing and Coding: Molecular Pathology and Genetic Testing Biomarkers for Oncology	A58917 L35396 A52986	JH - Novitas Solutions, Inc. JL - Novitas Solutions, Inc.	AR, CO, NM, OK, TX, LA, MS DE, DC, MD, NJ, PA
LCD LCA	Billing and Coding: MolDX: SEPT9 Gene Test Billing and Coding: MolDX: Testing of Multiple Genes MolDX: Defining panel services in MolDX MolDX: Inivata™, InvisionFirst®, Liquid Biopsy for Patients with Lung Cancer MolDX: Molecular Diagnostic Tests (MDT) MolDX: Phenotypic Biomarker Detection in Circulating Tumor Cells MolDX: Plasma-Based Genomic Profiling in Solid Tumors	A53702 A57503 A59678 L37870 A56924 L35025 A56853 L38566 A58021 L38043	JJ - Palmetto GBA JM - Palmetto GBA	AL, GA, TN NC, SC, VA, WV

		A57867		
LCA	Billing and Coding: Molecular Pathology and Genetic Testing	A58918	JN – First Coast Service Options, Inc.	FL, PR, US VI

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 detect cancer at an early stage. 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 ctDNA tests include, but may not be limited to, FoundationOne Liquid, Guardant360, Tempus xF; **OR**

- 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. Examples of CTC tests include, but may not be limited to, CellSearch

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.

Coverage Determination

iCare follows the Medicare requirements that only allow coverage and payment for services that are reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

CMS outlines coverage for items and services including molecular diagnostic tests (MDTs) and laboratory developed tests (LDTs) through National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs) and Local Coverage Articles (LCAs). iCare provides coverage for MDTs and LDTs identified as covered in an NCD, LCD or LCA when medical necessity criteria are met; however, ***for jurisdictions with no Medicare guidance about a specific MDT or LDT, iCare utilizes the DEX Diagnostics Exchange Registry (DEX) established by the Molecular Diagnostic Services Program (MolDX) as the standard to evaluate analytical and clinical validity and clinical utility.*** *MDTs and LDTs must meet analytical and clinical validity standards and demonstrate clinical utility to fulfill the CMS "reasonable and necessary" requirement. In the absence of clear CMS guidance, iCare may also develop and publish Medical Coverage Policies to determine medical necessity supported by generally accepted standards that are based on credible scientific evidence published*

in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas to determine medical necessity. An MDT or LDT must be ordered by a physician who is treating the beneficiary and the results must be used in the management of a beneficiary's specific medical problem.[44,86,87]

iCare applies any applicable National Coverage Determination (NCD) and any applicable Local Coverage Determinations (LCDs) to the services and jurisdiction at issue. See the Related CMS Documents Section above for any such NCDs or LCDs.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the criteria contained in the following:

~~Guardant360 Testing~~

~~Guardant360 (0326U)~~ ~~will be considered medically reasonable and necessary when all the following requirements are met:~~

- ~~Individual has been diagnosed with a recurrent, relapsed, refractory, metastatic, or advanced solid tumor that did not originate from the central nervous system. Individuals who would meet all of the indications on the Food & Drug Administration (FDA) label for larotrectinib if they are found to have a neurotrophic receptor tyrosine kinase (NTRK) mutation may be considered to have advanced cancer;~~ **~~AND~~**

- ~~Tissue-based, comprehensive genomic profiling (CGP) is infeasible (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;~~ **~~AND~~**

- ~~Individual has not previously been tested with the Guardant360 test for the same genetic content. For an individual who has been tested previously using Guardant360 for cancer, that individual may not be tested again unless there is clinical evidence that the cancer has evolved wherein testing would be performed for different genetic content. Specifically, in an individual with previously tested cancer, who have evidence of new malignant growth despite response to a prior targeted therapy, that growth may be considered sufficiently genetically different to require additional genetic testing;~~ **~~AND~~**

- ~~Individual is untreated for the cancer being tested, or the individual is not responding to treatment (eg, progression or new lesions on treatment);~~ **~~AND~~**

- ~~The individual has decided to seek further cancer treatment with the following conditions:~~

  - ~~Individual is a candidate for further treatment with a drug that is either FDA approved for the individual's cancer, or has a National Comprehensive Cancer Network (NCCN) 1 or NCCN 2A recommendation for that individual's cancer;~~ **~~AND~~**

  - ~~The FDA approved indication or NCCN recommendation is based upon information about the presence or absence of a genetic biomarker tested for in the Guardant360 assay~~

Circulating Tumor Cells Testing

For Jurisdictions without an LCD, iCare determines medical necessity for **circulating tumor cells (CTCs)** based on the criteria contained in:

- LCD – MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (L38643)

- LCA – Billing and Coding: MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (A58183)

~~**Circulating tumor cells (CTCs)** testing including, but not limited to, **CellSearch (86152, 86153)** will be considered medically reasonable and necessary when all the following requirements are met:~~

- ~~Individual has been diagnosed with cancer; **AND**~~

- ~~The specific cancer type has an associated biomarker that can be tested using CTCs; **AND**~~

- ~~Tissue based testing for the specific biomarker is infeasible (quantity not sufficient or invasive biopsy is medically contraindicated) **OR** will not provide sufficient information for subsequent medical management (eg, in cases where human epidermal growth factor receptor 2 (HER2) overexpression is negative in a tissue biopsy but may be positive in the CTCs, due to tumor heterogeneity). There is clear documentation of at least 1 of these reasons for testing in the medical record; **AND**~~

- ~~At least 1 of the following criteria are met AND there is clear documentation of at least 1 of these in the medical record:~~

  - ~~Individual's cancer has not previously been tested for the specific biomarker; **OR**~~

  - ~~Individual has newly metastatic cancer, and a metastatic lesion has not been tested for the specific biomarker; **OR**~~

  - ~~Individual demonstrates signs of clinical, radiological or pathologic disease progression; **OR**~~

  - ~~There is concern for resistance to treatment based on specific and well-established clinical indications; **AND**~~

- ~~The CTC-based biomarker test meets the following criteria to establish the test as reasonable and necessary:~~

  - ~~The clinical validation has demonstrated performance that is equivalent or superior to tissue-based testing or another already accepted test for the same biomarker for the same intended use; **AND**~~

  - ~~Clinical validity (for new analytes) must be established through studies published in the peer-reviewed literature for the intended use of the test in the intended population; **AND**~~

- For a given encounter, only 1 test for assessing the biomarker may be performed UNLESS a second test, meeting all the criteria established herein, is reasonable and necessary as an adjunct to the first test

InVisionFirst Testing

InVisionFirst (0388U) will be considered medically reasonable and necessary when the following requirements are met:

- Diagnosed with advanced (Stage IIIB/IV) NSCLC; **AND either of the following:**

At diagnosis:

- When results for *EGFR* single nucleotide variants (SNVs) and insertions and deletions (indels); rearrangements in *ALK* and *ROS1*; and SNVs for *BRAF* are not available; **AND**

- Tissue-based CGP is infeasible (quantity not sufficient for tissue-based CGP or invasive biopsy is medically contraindicated)

OR

At progression:

- For an individual progressing on or after chemotherapy or immunotherapy who have not been tested for *EGFR* SNVs and indels; rearrangements in *ALK* and *ROS1*; and SNVs for *BRAFs*, **AND**

    - Tissue-based CGP is infeasible; **OR**
    - Progression on EGFR tyrosine kinase inhibitors (TKIs)

General Liquid Biopsy Testing Criteria

Liquid biopsy (eg, cfDNA, ctDNA) including, but not limited to, **FoundationOne Liquid CDx (0239U), Guardant360 CDx (0242U)** will be considered medically reasonable and necessary when all the following requirements are met:

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

- Tissue-based, CGP is infeasible (quantity not sufficient for tissue-based CGP or invasive biopsy is medically contraindicated); **AND**

- Individual has not been previously tested with the same test using next generation sequencing (NGS) for the same cancer genetic content; **AND**

- Decided to seek further cancer treatment (eg, therapeutic chemotherapy); **AND**

- ~~The diagnostic laboratory test using NGS 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~~

Liquid Biopsy Testing

For jurisdictions without fully established guidance, **liquid biopsy (eg, cfDNA, ctDNA)** will be considered medically reasonable and necessary when the following indications are met:

- Individual diagnosed with either recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer[41]; **AND**
- Tissue based, comprehensive genomic profiling (CGP) is infeasible (quantity not sufficient for tissue based CGP or invasive biopsy is medically contraindicated) [41,89]; **AND**
- Individual has not been previously tested with the same test using next generation sequencing (NGS) for the same cancer genetic content[41]; **AND**
- Individual has decided to seek further cancer treatment with the following conditions[41]:
  - Drug is either FDA-approved for that individual's cancer, or has a National Comprehensive Cancer Network (NCCN) 1 or 2A recommendation for that individual's cancer[41]; **AND**
  - FDA-approved indication or NCCN recommendation is based upon information about the presence or absence of a genetic biomarker tested for in the test[41]

The use of the criteria above provides clinical benefits highly likely to outweigh any clinical harms (eg, adverse effects resulting from false-positive results and the subsequent need for further testing and biopsies, providing false reassurance to individuals who may have increased risks for developing cancer or emotional, social or financial consequences of test results[77]). Services that do not meet the criteria above are not medically reasonable and necessary and may result in unnecessary exposure to potential complications. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.

Coverage Limitations

US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage

The following services/items may not be considered a benefit (statutory exclusion)[86]:

- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law; **OR**
- Tests that confirm a diagnosis or known information; **OR**
- Tests to determine risk for developing a disease or condition; **OR**
- Tests performed to measure the quality of a process; **OR**
- Tests without diagnosis specific indications; **OR**
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial

These treatments and services fall within the Medicare program's statutory exclusion that prohibits payment for items and services that have not been demonstrated to be reasonable and necessary for the diagnosis and treatment of illness or injury (§1862(a)(1) of the Act).

For jurisdictions with no specific Medicare guidance about a specific MDT or LDT, the test is not covered UNLESS analytical validity, clinical validity and clinical utility have been established by one of the following[44,86,87]:

- MolDX Program approved technical assessment
- FDA approval/clearance performed within FDA labeling indications **AND** approved by the MolDX Program

The following services/items will not be considered medically reasonable and necessary:

- Liquid and solid tumor tissue testing for the same diagnosis and same genetic content
- Duplicate testing of the same biomarker (from the same sample type and for the same clinical indication) using different methodologies is not covered

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

Summary of Evidence

Molecular Diagnostic Tests (MDTs) and Lab Developed Tests (LDTs) without Molecular Diagnostic Services Program (MolDX) Approval or FDA Approval/Clearance

Medicare ensures a specific set of health benefits to eligible beneficiaries, meaning that Medicare is a defined benefit program. The Medicare Benefit Policy Manual (IOM 100-2, Ch. 15, Sec 10) identifies laboratory tests as a benefit category while the Social Security Act (Sec. 1862[a][1][A]) further defines what is covered by Medicare by stating that items and services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.[44,87,107]

An MDT is a type of medical test that involves the detection or identification of nucleic acids (deoxyribonucleic acid [DNA]/ribonucleic acid [RNA]), proteins, chromosomes, enzymes, cancer chemotherapy sensitivity and/or other metabolites. These tests look for specific changes in these molecules that may indicate the presence of a disease, an inherited condition or an individual's response to a particular medication. There are different types of MDTs, some of which may only involve analyzing a single gene for a specific variant (mutation). Others may involve more complex procedures and analyze multiple genes or molecules. In some cases, these tests may use algorithms or other forms of data evaluation to interpret results and assist with clinical decision making. An LDT is a medical test developed and performed by a specific laboratory. LDTs typically are not US Food and Drug Administration (FDA) approved/cleared.[28-32]

Under Medicare Benefit requirements, some types of tests may be denied as statutory exclusions and deemed as ineligible for coverage. This includes, but is not limited to, "tests identified as investigational by available literature and/or the literature supplied by the developer, and are not part of a clinical trial.[87]"

MDTs and LDTs must meet analytical and clinical validity standards and demonstrate clinical utility, which fulfills the CMS reasonable and necessary requirement for coverage. Analytical validity focuses on the technical performance of a test, referring to its accuracy and reliability in measuring what it is designed to measure. Clinical validity is the ability of a test to accurately identify or predict the presence or absence of a specific condition. Clinical utility refers to the usefulness of a test in improving clinical outcomes or guiding clinical decision-making. Even if a test is deemed safe and effective in terms of analytical and clinical validity, CMS mandates that the test must also be "reasonable and necessary" which is demonstrated by the test's clinical utility.[28 -32,80]

The MolDX Program was created to provide a process for determining if an MDT or LDT meets analytical and clinical validity criteria and demonstrates clinical utility at a level that meets the Medicare reasonable and necessary requirement. To this end, MolDX completes a Technical Assessment evaluation by reviewing best practices, societal guidelines, available evidence, technical reviews and expert opinion. Laboratories that perform FDA approved/cleared tests with proven utility and only perform the test within labeling indications may be exempt from the MolDX Technical Assessment. Following the Technical Assessment outcomes, the MolDX Program sets coverage determinations as follows: covered without restrictions beyond inherent design and purpose limitations, limited coverage (eg, for a specific diagnosis or clinical indication) or noncovered if the test was not deemed medically reasonable and necessary for the individual's diagnosis and/or treatment. The DEX Diagnostics Exchange Registry (DEX) is a centralized database of evaluated MDTs and LDTs and is publicly available.[87,88]

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	
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	
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	
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	
81479	Unlisted molecular pathology procedure	
81599	Unlisted multianalyte assay with algorithmic analysis	
82378	Carcinoembryonic antigen (CEA)	
86152	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood);	
86153	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood); physician interpretation and report, when required	
86304	Immunoassay for tumor antigen, quantitative; CA 125	
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	

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	
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)	
0229U	BCAT1 (Branched chain amino acid transaminase 1) or 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	
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	
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	

0337U	Oncology (plasma cell disorders and myeloma), circulating plasma cell immunologic selection, identification, morphological characterization, and	
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	
0343U	Oncology (prostate), exosome-based analysis of 442 small noncoding RNAs (sncRNAs) by quantitative reverse transcription polymerase chain reaction (RT-qPCR), urine, reported as molecular evidence of no-, low-, intermediate- or high-risk of prostate 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	
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	
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	
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), cellfree DNA (cfDNA), methylationbased 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	
0490U	Oncology (cutaneous or uveal melanoma), circulating tumor cell selection, morphological characterization and enumeration based on differential CD146, high molecular–weight melanoma-associated antigen, CD34 and CD45 protein biomarkers, peripheral blood	

0491U	Oncology (solid tumor), circulating tumor cell selection, morphological characterization and enumeration based on differential epithelial cell adhesion molecule (EpCAM), cytokeratins 8, 18, and 19, CD45 protein biomarkers, and quantification of estrogen receptor (ER) protein biomarker–expressing cells, peripheral blood	
0492U	Oncology (solid tumor), circulating tumor cell selection, morphological characterization and enumeration based on differential epithelial cell adhesion molecule (EpCAM), cytokeratins 8, 18, and 19, CD45 protein biomarkers, and quantification of PD-L1 protein biomarker–expressing cells, peripheral blood	
0496U	Oncology (colorectal), cell-free DNA, 8 genes for mutations, 7 genes for methylation by real-time RT-PCR, and 4 proteins by enzyme-linked immunosorbent assay, blood, reported positive or negative for colorectal cancer or advanced adenoma risk	
0501U	Oncology (colorectal), blood, quantitative measurement of cell-free DNA (cfDNA)	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

References

1. Aggarwal C, Thompson J, Black TA, et al. Clinical implications of plasma-based genotyping with the delivery of personalized therapy in metastatic non-small cell lung cancer. *JAMA Oncol*. 2019;5(2):173-180.

2. American College of Gastroenterology (ACG). ACG Clinical Guidelines: colorectal cancer screening 2021. https://gi.org. Published March 2021.

3. American College of Gastroenterology (ACG). Colorectal cancer screening: U.S. multi-society task force on colorectal cancer. https://gi.org. Published January 2022.

4. American Society of Clinical Oncology (ASCO). Biomarkers for adjuvant endocrine and chemotherapy in early-stage breast cancer: ASCO guideline update. https://www.asco.org. Published April 19, 2022.

5. American Society of Clinical Oncology (ASCO). Circulating tumor DNA analysis in patients with cancer: American Society of Clinical Oncology and College of American Pathologists joint review. https://www.asco.org. Published March 5, 2018.

6. American Society of Clinical Oncology (ASCO). Endocrine treatment and targeted therapy for HR-positive, HER2-negative metastatic breast cancer guideline and rapid update. https://www.asco.org. Published February 6, 2024.

7. American Society of Clinical Oncology (ASCO). Somatic genomic testing in patients with metastatic or advanced cancer: ASCO provisional clinical opinion. https://www.asco.org. Published February 17, 2022.

8. American Society of Colon and Rectal Surgeons (ASCRS). The American Society of Colon and Rectal Surgeons clinical practice guidelines for the management of colon cancer. https://www.fascrs.org. Published February 2022.

9. Association for Molecular Pathology (AMP). Do circulating tumor cells, exosomes, and circulating tumor nucleic acids have clinical utility? https://www.amp.org. Published May 2015.

10. Association for Molecular Pathology (AMP). Molecular biomarkers for the evaluation of colorectal carcinoma: guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. https://www.amp.org. Published February 6, 2017.

11. Association for Molecular Pathology (AMP). Recommendations for cell-free DNA assay validations. A joint consensus recommendation of the Association for Molecular Pathology and College of American Pathologists. https://www.amp.org. Published October 6, 2023.

12. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (A56867). https://www.cms.gov. Published August 15, 2019. Updated July 1, 2024.

13. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: Billing and Coding: Guardant360® (A58192). https://www.cms.gov. Published May 15, 2020.

14. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: Guardant360® (A58214). https://www.cms.gov. Published May 15, 2020.

15. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: Molecular pathology and genetic testing (A58917). https://www.cms.gov. Published November 8, 2021. Updated July 1, 2024.

16. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: Molecular pathology and genetic testing (A58918). https://www.cms.gov. Published November 8, 2021. Updated July 1, 2024.

17. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding:

MolDx: SEPT9 Gene Test (A53702). https://www.cms.gov. Published October 1, 2015. Updated November 21, 2019.

18. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: MolDx: SEPT9 Gene Test (A55206). https://www.cms.gov. Published February 16, 2017. Updated November 30, 2023.

19. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: MolDx: SEPT9 Gene Test (A54300). https://www.cms.gov. Published October 1, 2015. Updated November 16, 2023.

20. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: MolDx: SEPT9 Gene Test (A55623). https://www.cms.gov. Published October 9, 2017. Updated December 17, 2021.

21. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: MolDx: SEPT9 Gene Test (A55628). https://www.cms.gov. Published October 9, 2017. Updated December 17, 2021.

22. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCD). Biomarkers for Oncology (L35396). https://www.cms.gov. Published October 1, 2015. Updated December 13, 2020.

23. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Inivata™, InvisionFirst®, liquid biopsy for patients with lung cancer (L37870). https://www.cms.gov. Published April 8, 2019. Updated October 14, 2021.

24. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Inivata™, InvisionFirst®, liquid biopsy for patients with lung cancer (L37897). https://www.cms.gov. Published June 3, 2019. Updated October 14, 2021.

25. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Inivata™, InvisionFirst®, liquid biopsy for patients with lung cancer (L37899). https://www.cms.gov. Published June 3, 2019. Updated October 14, 2021.

26. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Inivata™, InvisionFirst®, liquid biopsy for patients with lung cancer (L37903). https://www.cms.gov. Published May 13, 2019. Updated June 27, 2024.

27. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Inivata™, InvisionFirst®, liquid biopsy for patients with lung cancer (L37921). https://www.cms.gov. Published April 15, 2019. Updated November 30, 2023.

28. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L36256). https://www.cms.gov. Published October 1, 2015. Updated May 4, 2023.

29. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX:

molecular diagnostic tests (MDT) (L36021). https://www.cms.gov. Published October 1, 2015. Updated May 4, 2023.

30. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L35160). https://www.cms.gov. Published October 1, 2015. Updated May 4, 2023.

31. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L35025). https://www.cms.gov. Published October 1, 2015. Updated May 4, 2023.

32. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L36807). https://www.cms.gov. Published February 16, 2017. Updated April 27, 2023.

33. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: phenotypic biomarker detection in circulating tumor cells (L38566). https://www.cms.gov. Published July 25, 2021. Updated May 26, 2022.

34. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: phenotypic biomarker detection in circulating tumor cells (L38584). https://www.cms.gov. Published July 25, 2021. Updated May 16, 2024.

35. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: phenotypic biomarker detection in circulating tumor cells (L38643). https://www.cms.gov. Published July 4, 2021. Updated June 2, 2022.

36. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: phenotypic biomarker detection in circulating tumor cells (L38645). https://www.cms.gov. Published July 4, 2021. Updated June 2, 2022.

37. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: phenotypic biomarker detection in circulating tumor cells (L38678). https://www.cms.gov. Published July 25, 2021. Updated May 26, 2022.

38. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: plasma-based genomic profiling in solid tumors (L38043). https://www.cms.gov. Published February 3, 2020. Updated December 30, 2021.

39. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: plasma-based genomic profiling in solid tumors (L38065). https://www.cms.gov. Published July 27, 2020. Updated October 26, 2023.

40. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: plasma-based genomic profiling in solid tumors (L38168). https://www.cms.gov. Published March 15, 2020. October 26, 2023.

41. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: plasma-based genomic profiling in solid tumors (L39230). https://www.cms.gov. Published December 26, 2022.

42. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: plasma-based genomic profiling in solid tumors (L39232). https://www.cms.gov. Published December 26, 2022.

43. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Molecular Pathology Procedures (L35000). https://www.cms.gov. Published October 1, 2015. Updated August 1, 2024.

44. Centers for Medicare & Medicaid Services (CMS). Medicare benefit policy manual: chapter 15 - covered medical and other health services. https://www.cms.gov. Updated March 7, 2024.

45. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD). Next generation sequencing (NGS) (90.2). https://www.cms.gov. Published January 27, 2020.

46. College of American Pathologists (CAP). Updated molecular testing guideline for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors: guideline from the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. https://www.cap.org. Updated March 2018.

47. ECRI Institute. ECRIgene Genetic Test Assessment. CellSearch CTC Test (Menarini Silicone Biosystems, Inc.) for monitoring metastatic breast cancer treatment response and evaluating prognosis. https://www.ecri.org. Published June 2020.

48. ECRI Institute. ECRIgene Genetic Test Assessment. CellSearch CTC Test (Menarini Silicone Biosystems, Inc.) for monitoring metastatic colorectal cancer treatment response and evaluating prognosis. https://www.ecri.org. Published June 2020.

49. ECRI Institute. ECRIgene Genetic Test Assessment. Colvera (Clinical Genomics Pathology, Inc.) liquid biopsy test to monitor for recurrent colorectal cancer. https://www.ecri.org. Published October 21, 2021.

50. ECRI Institute. ECRIgene Genetic Test Assessment. FirstSightCRC (CellMax Life) for colorectal cancer screening. https://www.ecri.org. Published June 2021.

51. ECRI Institute. ECRIgene Genetic Test Assessment. FoundationOne liquid (Foundation Medicine, Inc.) genomic profiling and liquid biopsy test for guiding targeted therapy for solid tumors. https://www.ecri.org. Published September 3, 2019.

52. ECRI Institute. ECRIgene Genetic Test Assessment. Galleri Multicancer Early Detection Test (Grail, LLC) for cancer screening. https://www.ecri.org. Published February 2024.

53. ECRI Institute. ECRIgene Genetic Test Assessment. GeneStrat (Biodesix, Inc.) liquid biopsy test to guide targeted therapy for non-small cell lung cancer. https://www.ecri.org. Published October 21,

2021.

54. ECRI Institute. ECRIgene Genetic Test Assessment. Guardant360 (Guardant Health, Inc.) test for informing management of advanced solid tumor cancers. https://www.ecri.org. Published August 2020.

55. ECRI Institute. ECRIgene Genetic Test Assessment. InVisionFirst-Lung (Inivata Ltd) genomic profiling and liquid biopsy test for guiding targeted therapy for non-small cell lung cancer. https://www.ecri.org. Published June 2021.

56. ECRI Institute. ECRIgene Genetic Test Assessment. Tempus xF (Tempus) to guide targeted therapy for solid tumor cancers. https://www.ecri.org. Published October 2020.

57. ECRI Institute. ECRIgene Genetic Test Product Brief. GPS cancer test (NantHealth, Inc.) for informing management of solid tumors. https://www.ecri.org. Published March 2017.

58. ECRI Institute. ECRIgene Genetic Test Product Brief. Trovera BRAF (Trovagene, Inc.) liquid biopsy test for informing management of BRAF-associated disorders. https://www.ecri.org. Published November 2016.

59. ECRI Institute. ECRIgene Genetic Test Product Brief. Trovera KRAS (Trovagene, Inc.) liquid biopsy test for informing management of KRAS-associated cancers. https://www.ecri.org. Published March 2017.

60. Hayes, Inc. Clinical Utility Evaluation. Liquid biopsy tests for colorectal cancer screening. https://evidence.hayesinc.com. Published March 26, 2020. Updated March 30, 2023.

61. Hayes, Inc. Genetic Test Evaluation (GTE) Synopsis. GPS Cancer (NantHealth). https://evidence.hayesinc.com. Published February 2, 2017.

62. Hayes, Inc. Health Technology Brief (ARCHIVED). CellSearch circulating tumor cell (CTC) Kit (Janssen Diagnostics LLC) for monitoring metastatic breast cancer. https://evidence.hayesinc.com. Published October 23, 2014. Updated August 31, 2016.

63. Hayes, Inc. Molecular Test Assessment. ColonSentry (Stage Zero Life Sciences). https://evidence.hayesinc.com. Published December 11, 2018. Updated June 22, 2023.

64. Hayes, Inc. Molecular Test Assessment. Colvera (Clinical Genomics Pathology Inc.). https://evidence.hayesinc.com. Published November 14, 2018. Updated July 1, 2022.

65. Hayes, Inc. Molecular Test Assessment. Epi proColon (Epigenomics Inc.). https://evidence.hayesinc.com. Published September 30, 2020. Updated October 14, 2022.

66. Hayes, Inc. Molecular Test Assessment. FirstSight^{CRC} (CellMax Life).

https://evidence.hayesinc.com. Published August 7, 2020. Updated September 27, 2023.

67. Hayes, Inc. Molecular Test Assessment. FoundationOne Liquid (Foundation Medicine Inc.). https://evidence.hayesinc.com. Published June 13, 2019.

68. Hayes, Inc. Molecular Test Assessment. FoundationOne Liquid CDx (Foundation Medicine Inc.). https://evidence.hayesinc.com. Published November 30, 2023.

69. Hayes, Inc. Molecular Test Assessment. GeneStrat (Biodesix Inc.). https://evidence.hayesinc.com. Published December 5, 2017. Updated June 3, 2024.

70. Hayes, Inc. Molecular Test Assessment. Guardant360 and Guardant360 CDx (Guardant Health Inc.). https://evidence.hayesinc.com. Published August 1, 2024.

71. Hayes, Inc. Precision Medicine Research Brief. Comprehensive molecular profiling of circulating solid tumor DNA for the intended use as a broad molecular profiling tool for monitoring. https://evidence.hayesinc.com. Published October 18, 2022.

72. Hayes, Inc. Precision Medicine Research Brief. Comprehensive molecular profiling of circulating solid tumor DNA for the intended use as a broad molecular profiling tool to aid treatment selection. https://evidence.hayesinc.com. Published October 18, 2022.

73. Hayes, Inc. Precision Medicine Research Brief. RadTox cfDNA Test (DiaCarta Inc.). https://evidence.hayesinc.com. Published December 7, 2022.

74. Katz R, Zaidi T, Pujara D, et al. Identification of circulating tumor cells using 4-color fluorescence in situ hybridization: Validation of a noninvasive aid for ruling out lung cancer in patients with low-dose computed tomography-detected lung nodules. *Cancer Cytopathol.* 2020;128(8):553-562.

75. Li N, Wang B, Li J, et al. Perioperative circulating tumor DNA as a potential prognostic marker for operable stage I to IIIA non-small cell lung cancer. *Cancer*. 2022;128(4):708-718.

76. Lyu X, Tsui Y, Ho D, et al. Liquid biopsy using cell-free or circulating tumor DNA in the management of hepatocellular carcinoma. *Cell Mol Gastroenterol Hepatol*. 2022;13(6):1611-1624.

77. MedlinePlus. What are the risks and limitations of genetic testing? https://medlineplus.gov. Updated July 28, 2021.

~~78. MCG Health. Emerging Guidelines Preview. Oncology companion diagnostic testing – Guardant360 CDx. https://humana.access.mcg.com/index. Published November 4, 2022.~~

~~79. MCG Health. Septin 9 (SEPT9) DNA methylation testing. https://humana.access.mcg.com/index.~~

80. National Academies of Sciences, Engineering and Medicine. An evidence framework for genetic testing. https://www.ncbi.nlm.nih.gov. Published 2017.

81. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Breast cancer. https://www.nccn.org. Updated July 3, 2024.

82. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colon cancer. https://www.nccn.org. Updated August 22, 2024.

83. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colorectal cancer screening. https://www.nccn.org. Updated February 27, 2024.

84. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Multiple myeloma. https://www.nccn.org. Updated April 26, 2024.

85. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. https://www.nccn.org. Updated August 23, 2024.

86. Palmetto GBA. Molecular diagnostic program (MolDX): coverage, coding, and pricing standards and requirements (M00106). https://www.palmettogba.com/MolDx. Published December 2019.

87. Palmetto GBA. Molecular diagnostic tests and Medicare. https://www.palmettogba.com . Published June 23, 2023.

88. Patient-Centered Outcomes Research Institute. (PCORI). Emerging technologies and therapeutics report: genomic sequencing to guide cancer management. https://www.pcori.org. Published June 2021. Updated June 28, 2024.

89. Rozenblum AB, Ilouze M, Dudnik E, et al. Clinical impact of hybrid capture-based next-generation sequencing on changes in treatment decisions in lung cancer. *J Thorac Oncol.* 2017;12(2):258-268.

90. Rolfo C, Mack P, Scagliotti G, et al. Liquid biopsy for advanced NSCLC: a consensus statement from the International Association for the Study of Lung Cancer. *J Thorac Oncol*. 2021;16(10):1647-1662.

91. Tie J, Cohen J, Lahouel K, et al. Circulating tumor DNA analysis guiding adjuvant therapy in stage II colon cancer. *N Engl J Med.* 2022;386(24):2261-2272.

92. UpToDate, Inc. Assessment of tumor response in patients receiving systemic and nonsurgical

locoregional treatment of hepatocellular cancer. https://www.uptodate.com. Updated July 2024.

93. UpToDate, Inc. Multiple myeloma: clinical features, laboratory manifestations, and diagnosis. https://www.uptodate.com. Updated July 2024.

94. UpToDate, Inc. Personalized, genotype-directed therapy for advanced non-small cell lung cancer. https://www.uptodate.com. Updated July 2024.

95. UpToDate, Inc. Post treatment surveillance after colorectal cancer resection. https://www.uptodate.com. Updated July 2024.

96. UpToDate, Inc. Prognostic and predictive factors in metastatic breast cancer. https://www.uptodate.com. Updated July 2024.

97. UpToDate, Inc. Systemic therapy for metastatic colorectal cancer: General principles. https://www.uptodate.com. Updated July 2024

98. UpToDate, Inc. Test for screening for colorectal cancer. https://www.uptodate.com. Updated July 2024.

99. UpToDate, Inc. Treatment for hormone receptor-positive, HER2-negative breast advanced cancer. https://www.uptodate.com. Updated July 2024.

100. UpToDate, Inc. Tumor, node, metastasis (TNM) staging system and other prognostic factors in cutaneous melanoma. https://www.uptodate.com. Updated July 2024.

101. US Food & Drug Administration (FDA). 510(k) summary: Cellsearch circulating tumor cell kit. https://www.fda.gov. Published December 21, 2010.

102. US Food & Drug Administration (FDA). List of cleared or approved companion diagnostic devices (in vitro and imaging tools). https://www.fda.gov. Updated May 1, 2024.

103. US Food & Drug Administration (FDA). Premarket approval (PMA): FoundationOne Liquid CDx. https://www.fda.gov. Published September 1, 2020. Updated July 25, 2023.

104. US Food & Drug Administration (FDA). Premarket approval (PMA): Guardant360 CDx. https://www.fda.gov. Published August 28, 2020. Updated January 27, 2023.

105. US Food & Drug Administration (FDA). Summary of safety and effectiveness data: Agilent Resolution CtDx FIRST. https://www.fda.gov. Published December 12, 2022.

106. US Food & Drug Administration (FDA). Summary of safety and effectiveness data: Epi proColon. https://www.fda.gov. Published April 23, 2016.

107. US Congress. United States Code: Social Security Act, 42 U.S.C. §§ 301- 1940. Sec.

1862(a)(1)(A): exclusions from coverage and Medicare as a secondary payer. https://www.ssa.gov. Published 1940.

Change Summary

01/01/2024 New Policy.
03/26/2024 Update, No Coverage Change.
07/01/2024 Provider Claims Codes Update, No Coverage Change.
08/06/2024 Update, No Coverage Change.
10/08/2024 Annual Review, Coverage Change.