Medicare Medical Policy

Circulating Tumor Cell and DNA Assays for Cancer Management

MEDICARE MEDICAL POLICY NUMBER: 306

Effective Date: 8/1/2024

Last Review Date: 7/2024

Next Annual Review: 7/2025

INSTRUCTIONS FOR USE: Company Medicare Medical Policies serve as guidance for the administration of plan benefits and do not constitute medical advice nor a guarantee of coverage. Company Medicare Medical Policies are reviewed annually to guide the coverage or non-coverage decision-making process for services or procedures in accordance with member benefit contracts (otherwise known as Evidence of Coverage or EOCs) and Centers of Medicare and Medicaid Services (CMS) policies, manuals, and other CMS rules and regulations. In the absence of a CMS coverage determination or specific regulation for a requested service, item or procedure, Company policy criteria or applicable utilization management vendor criteria may be applied. These are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

The Company reserves the right to determine the application of Medicare Medical Policies and make revisions to these policies at any time. Any conflict or variance between the EOC and Company Medical Policy will be resolved in favor of the EOC.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PRODUCT AND BENEFIT APPLICATION

☒ Medicare Only

MEDICARE COVERAGE CRITERIA

IMPORTANT NOTE: More than one Centers for Medicare and Medicaid Services (CMS) reference may apply to the same health care service, such as when more than one coverage policy is available (e.g., both an NCD and LCD exist). All references listed should be considered for coverage decision-making. The Company uses the most current version of a Medicare reference available at the time of publication; however, these websites are not maintained by the Company, so Medicare references and their corresponding hyperlinks may change at any time. If there is a conflict between the Company Medicare Medical Policy and CMS guidance, the CMS guidance will govern.

Service	Medicare Guidelines
Circulating Tumor Cell (CTC) Testing	• **Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, and WY:** Local Coverage Determination (LCD) for MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (L38645) • **Testing performed in CA and NV:** LCD for MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (L38643) *If a test is not specifically included in a policy, additional research may be required to ensure all elements of the LCD are met for coverage.*
Next Generation Sequencing– ***Plasma-Based Tests Subject to NCD 90.2***	National Coverage Determination (NCD) for Next Generation Sequencing (NGS) (90.2) **NOTE:** Relevant tests subject to this NCD include the following: • FoundationOne®Liquid CDx (0239U or 81479, the latter code used for claims prior to 7/1/2020) (Foundation Medicine) • Guardant360® CDx (0242U) (Guardant Health, Redwood City, CA) *(See additional rows below as well as "Policy Guidelines" for notes regarding other Guardant360 test options.)* • As of 12/12/2022: Agilent Resolution ctDx FIRST (0397U) (Resolution Bioscience, Inc., Kirkland, WA) *See "Policy Guidelines" below for important information regarding the NCD 90.2*

InVisionFirst®-Lung (0388U)	LCD for MolDX: Inivata™, InvisionFirst®, Liquid Biopsy for Patients with Lung Cancer (L37899)
Plasma Based (liquid biopsy) Genetic Testing Not Otherwise Specified in the Policy	For the Guardant360 LDT® (0326U): • Local Coverage Article (LCA): Billing and Coding: Guardant360® (A58192) *(The FDA approved CDx test is addressed separately)* For all other plasma-based (liquid biopsy) tests: • **Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, and WY:** LCD: MolDX: Plasma-Based Genomic Profiling in Solid Tumors (L39232) • **Testing performed in CA and NV:** LCD: MolDX: Plasma-Based Genomic Profiling in Solid Tumors (L39230) • **Testing performed in NC, SC, AL, GA, VA, and WV:** LCD: MolDX: Plasma-Based Genomic Profiling in Solid Tumors (L38043) **NOTES:** According to the above LCDs, "Other liquid biopsies will be covered for the same indications if they display similar performance in their intended used applications to Guardant360®." Therefore, liquid biopsy tests **other than** Guardant360® may also be medically necessary; however, if a test is not specifically called out in a policy, additional research is required to confirm Medicare coverage as not all liquid biopsy tests will meet LCD requirements. Other tests which may be **medically necessary** when LCD criteria are met include, but may not be limited to, the following: • Guardant360 Response™ (Guardant Health) (Code 0422U) • LiquidHALLMARK® (Lucence Health, Inc.; California) (Code 0409U) • Epic Sciences ctDNA Metastatic Breast Cancer Panel (Epic Sciences, Inc.; California) (0428U)
	These tests are considered **not medically necessary**, based on Medicare guidelines (see *"Policy Guidelines"* below) and the above LCD(s). • The Resolution ctDx Lung™ (Resolution Bioscience, Inc., Kirkland, WA) (Code 0179U) (This test/code is also noted as "not covered" within the LCA A58975) • LungLB® (LungLife AI®; California) (Code 0317U) • HelioLiver™ Test (Fulgent Genetics, LLC and Helio Health Inc.; California) (Code 0333U)

	• RadTox™ cfDNA test (DiaCarta Clinical Lab; California) (Code 0285U) • ColoScape™ Colorectal Cancer Detection cfDNA test (DiaCarta Clinical Lab; California) (Code 0368U) • OncobiotaLUNG (Micronoma™; California) (Code 0395U) • Prior to 12/12/2022: Agilent Resolution ctDx FIRST (Resolution Bioscience, Inc., Kirkland, WA) (Code 0397U) • DiviTum®TKa (Biovica Inc.; California) (Code 0404U) • BTG Early Detection of Pancreatic Cancer (Breakthrough Genomics; California) (Code 0405U) • ColonAiQ® (Breakthrough Genomics) (Code 0453U) *If a test is not specifically included in a policy, additional research may be required.*
PIK3CA Gene Tests	**Testing performed in NC, SC, AL, GA, VA, WV, AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA and NV:** LCA: Billing and Coding: MolDX: PIK3CA Gene Tests (A55200)
Colvera (Code 0229U)	LCA for Billing and Coding: Biomarkers for Oncology (A52986)
NavDx® (Naveris, Inc.; Massachusetts or North Carolina) (Code 0356U)	LCD for MolDX: Minimal Residual Disease Testing for Cancer (L38779) **NOTES:** • For more information about MRD testing, see the separate Medicare medical policy for *Next Generation Sequencing for Minimal Residual Disease Detection*. • The NavDx® test is listed as in the DEX® Registry under Naveris as "Covered," under both a North Carolina and Massachusetts location. While the MAC over Massachusetts (National Government Services) does not use MoDX outcomes, the MAC over North Carolina (Palmetto J-M) does, and since coverage is potentially favorable for this latter service area using MolDX guidelines, we will use the noted North Carolina LCD for this test, for testing performed in **any** location.
Medicare Coverage Criteria: "MA organizations may create publicly accessible internal coverage criteria… when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs." *(§ 422.101(b)(6) – see Policy Guidelines below*) • **Medicare Coverage Manuals:** Medicare does not have criteria for circulating tumor cells (CTCs) or circulating tumor/cell-free DNA (ctDNA or cfDNA) testing in a coverage manual. **However, broad coverage requirements are provided by Medicare for diagnostic laboratory testing in general.** Specifically, Medicare requires diagnostic laboratory tests be ordered by a provider who is treating the member for a specific medical problem and who will promptly use the test results in the direct management of that specific medical problem.[1,2] These coverage criteria are considered "not fully established" under CFR § 422.101(6)(i)(A) as	

additional criteria are needed to interpret or supplement these general coverage provisions in order to determine medical necessity consistently. • **National Coverage Determination (NCD):** Other than tests noted above that use NCD 90.2, most tests are not subject to this NCD (this NCD only applies to certain tests, and for certain indications), and no other NCD for ctDNA or CTC testing is available. • **Local Coverage Determination (LCD)/Local Coverage Article (LCA):** According to Medicare guidelines, "Jurisdiction of payment requests for laboratory services furnished by an independent laboratory… lies with the A/B MAC (B) serving the area in which the laboratory test is performed."[3] The ctDNA and CTC tests identified below do **not** have an available LCD or LCA for their respective service areas (the MACs for Pennsylvania and Massachusetts are Novitas Solutions and National Government Services, respectively). • Therefore, in the absence of established Medicare coverage criteria in a manual, NCD, LCD, or other regulatory guidance for the service area in which the testing is being performed, Company criteria below are applied for medical necessity decision-making. Medicare statutes and regulation provide general coverage criteria for diagnostic testing, but additional criteria to interpret or supplement the Medicare criteria are being used in order to determine medical necessity consistently. These additional criteria provide clinical benefits that are highly likely to outweigh any clinical harms, including from delayed or decreased access to items or services **because the use of this additional criteria based on peer-reviewed evidence evaluates how testing is expected to improve diagnosis, improve patient management, change treatment decisions or improve health outcomes**. Specifically, the literature review is used to evaluate whether or not each test has established clinical utility and/or analytic validity. Tests without proven clinical utility and/or analytical validity pose risk to patients due to high false positive or false negative test results. False positives can lead to an individual undergoing an unnecessary invasive procedure, and false negatives may result in the selection of ineffective treatments, or treatment not being initiated in a timely manner. • ***NOTE:*** *The summary of evidence, as well as the list of citations/references used in the development of the Company's internal coverage criteria, are publicly available and can be found using the Company medical policy link below [CFR § 422.101(6)(ii)(A) and (B)].*	
Tests Not Otherwise Addressed *Examples:* • *CELLSEARCH® Circulating Multiple Myeloma Cell (CMMC) Test (Menarini Silicon Biosystems, Inc.; Pennsylvania) (Code 0337U)* • *CELLSEARCH® HER2 Circulating Tumor Cell (CTC-HER2) Test (Menarini Silicon Biosystems, Inc.; Pennsylvania) (Code 0338U)* • *IMMray® PanCan-d (Immunovia, Inc.; Massachusetts) (Code 0342U)*	Company medical policy for Circulating Tumor Cell and DNA Assays for Cancer Management I. These services are considered **not medically necessary** for Medicare based on the Company medical policy. *See Policy Guidelines below.*

IMPORTANT NOTICE: While some services or items may appear medically indicated for an individual, they may also be a direct exclusion of Medicare or the member's benefit plan. Such excluded services or items by Medicare and member EOCs include, but are not limited to, services or procedures considered to be cosmetic, not medical in nature, or those considered not medically reasonable or necessary under *Title XVIII of the Social Security Act, §1862(a)(1)(A).* If there is uncertainty regarding coverage of a service or item, please review the member EOC or submit a pre-service organization determination request. Note that the Medicare Advance Beneficiary Notice of Noncoverage (ABN) form **cannot** be used for Medicare Advantage members. *(Medicare Advance Written Notices of Non-coverage. MLN006266 May 2021)*

POLICY CROSS REFERENCES

MEDICAL POLICIES

- Genetic and Molecular Testing, MP317

PHARMACY POLICIES

- Injectable ANTI-Cancer Medications. Antineoplastics, ORPTCONC102
- Oral ANTI-Cancer Medications. Antineoplastics, ORPTCONC103

The full Company portfolio of Medicare Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

DOCUMENTATION REQUIREMENTS

In order to review for medical necessity under *Social Security Act, §1862(a)(1)(A),* the following documentation **must** be provided. If any of these items are not submitted, the review may be delayed, and the decision outcome could be affected:

- Laboratory name and location.
- Test name (if appropriate, the proprietary test name, especially for panel tests) and relevant CPT code(s)
    - Non-specific (e.g., 81401, 81402, etc.) or unlisted (e.g., 81479) CPT codes are not sufficient to satisfy this requirement alone. Test/gene description or name is required.
- Documented diagnosis of a recurrent, relapsed, refractory, metastatic, or advanced solid tumor.
- Documentation of any prior genetic or molecular testing performed for the individual.
- Documentation of cancer treatments being considered for the individual, meeting both of the following:
    - The patient must be a candidate for further treatment; and
    - The drug must be:
        - FDA-approved for that patient's cancer ***OR*** have a National Comprehensive Cancer Network (NCCN) 1 or NCCN 2A recommendation for that patient's cancer, and
        - The FDA-approved indication or NCCN recommendation must be based on information about the presence or absence of a genetic biomarker tested for in

the test (i.e., the medication being considered must be indicated for tumors that rely on relevant gene mutation or variant test results. Medications or cancer treatment that are not dependent on genetic test results would not require the use of genetic testing to proceed with such treatment decisions, thus resulting in genetic testing not being medically necessary to proceed with such treatments).

- Documentation of either no prior cancer treatments for the cancer being tested ***OR*** documentation of prior cancer treatments that have been used with the noted response to those treatments.
- Tissue based testing:
    - Documentation must support tissue-based, comprehensive genomic profiling (CGP) is infeasible (e.g., quantity not sufficient for tissue-based CGP or invasive biopsy is medically contraindicated); or
    - For NSLC, documentation that tissue-based CGP did not show actionable mutations.

GUARDANT360® TESTS

Guardant offers multiple "Guardant360®" test options. Only the Guardant360® CDx test has been **FDA approved** (as of August 2020). All other Guardant tests are lab-developed tests without FDA approval and thus, would be subject to Medicare contractor/MolDX Program review.

Note that the Guardant360 TissueNext™ test is **not** a liquid biopsy, and therefore, this medical policy would **not** apply to this particular Guardant360 test.

IMPORTANT INFORMATION REGARDING NEXT GENERATION SEQUENCING (NGS) TESTS AND NCD 90.2

The Medicare national coverage determination (NCD) 90.2 does **not** apply to all NGS tests. The scope of this NCD is limited to next generation sequencing tests, NGS *DNA* sequencing tests that are used for cancer-related purposes and only tests which have received FDA-approval or clearance as a companion diagnostic (CDx) test (see Criteria 1b and 2b of the NCD). The FDA website "List of Cleared or Approved Companion Diagnostic Devices" provides the most current listing of FDA-approved or cleared tests.

Other NGS tests are **not** subject to this NCD. This includes:

- Tests which are not next generation sequencing tests;
- Tests which do not have FDA-approval or clearance as CDx tests;
- NGS *RNA* sequencing tests; and
- Tests related to *non*-cancer indications.

The Agilent Resolution ctDx FIRST test (PLA code 0397U), by Resolution Bioscience, Inc., Kirkland, WA, was not FDA approved as a CDx until December 12, 2022. Therefore, it is not eligible for coverage under the NCD 90.2 until this date.

Coverage of tests which are not subject to the NCD is left to local Medicare Contractor (MAC) discretion. Some tests may or may not have a specific LCD or LCA available, while others are subject to more generalized requirements. See Medicare references in the "Criteria" table above or separate Medicare

policies. If a test is not specifically included in a policy, additional research may be required to confirm coverage under Medicare.

MEDICARE AND MEDICAL NECESSITY FOR DIAGNOSTIC LABORATORY SERVICES

States subject to the Medicare Molecular Diagnostics (MolDX) Program

Laboratories performing tests in service areas which have adopted guidelines or coverage determinations made by the Medicare Molecular Diagnostics (MolDX) Program contractor are required to submit a technology assessment (TA) to establish analytical and clinical validity (AV/CV) and clinical utility (CU). Supporting LCDs regarding TA reviews include, but are not limited to, the following:

- Laboratories in CA & NV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35160)
- Laboratories in NC, SC, GA, TN, AL, VA, & WV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35025)
- Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, & WY: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L36256)

Coverage or non-coverage determinations made by MolDX are maintained in the DEX™ Diagnostics Exchange registry catalog and are available for public viewing. If a test does not have a coverage determination by the MolDX Program, then AV/CV and CU have **not** been established and the test is considered not medically reasonable and necessary under *SSA §1862(a)(1)(A)* until a MolDX review is complete and coverage is indicated by MolDX or Noridian. Therefore, tests identified in this policy as not meeting this requirement are not medically reasonable or necessary for Medicare under *SSA §1862(a)(1)(A).* This includes both the RadTox™ cfDNA test and the ColoScape™ Colorectal Cancer Detection cfDNA test, both by DiaCarta Clinical Lab in California. These tests are listed in the DEX Registry as "Not covered" for Medicare which means these tests have had their clinical utility and analytical validity (CU/AV) assessed and were determined to be not medically reasonable or necessary for Medicare under *Social Security Act, §1862(a)(1)(A).* These and other related tests include those found in Table 1 below.

Note: This list was accurate at the time of publication, but it is subject to change at any time by the Medicare MolDX Program contractor.

Table 1: Related tests

Proprietary Test Name	Laboratory	MolDX TA Review Outcome (as found in the DEX™ Diagnostics Exchange registry)
RadTox™ cfDNA test (0285U)	DiaCarta Clinical Lab (California)	Not Covered
ColoScape™ Colorectal Cancer Detection cfDNA test (0368U)	DiaCarta Clinical Lab (California)	Not Covered
Guardant360 LDT® (0326U)	Guardant Health (California)	Covered
LungLB® (Code 0317U)	LungLife AI® (California)	Not Covered
HelioLiver™ Test (0333U)	Fulgent Genetics, LLC and Helio Health Inc. (California)	Not Covered
OncobiotaLUNG (0395U)	Micronoma™ (California)	Not Covered

Agilent Resolution ctDx FIRST (0397U)	Resolution Bioscience, Inc. (Kirkland, WA)	Not Covered (Prior to 12/12/2022; After 12/12/2022, NCD 90.2 applies)
BTG Early Detection of Pancreatic Cancer (0405U)	Breakthrough Genomics (California)	Not Covered (No TA performed as of this policy update)
LiquidHALLMARK® (0409U)	Lucence Health, Inc. (California)	Covered
Guardant360 Response™	Guardant Health (California)	Covered
ColonAiQ® (0453U)	Breakthrough Genomics	Not Covered (No TA performed as of this policy update)
DiviTum®TKa (0404U)	Biovica Inc. (California)	Not Covered (No TA performed as of this policy update)
The Resolution ctDx Lung™ (0179U)	Resolution Bioscience, Inc. (Kirkland, WA)	Not Covered (Listed as "not covered" in registry)

Non-Molecular or Genetic Tests

The Medicare MolDX Program only applies to molecular and genetic tests. Other types of tests, such as tumor antigen testing, are not subject to MolDX guidelines. In the absence of an available NCD or LCD/LCA, these tests will follow Company policy criteria with regards to clinical and analytical validity, as well as clinical utility, which is required to establish Medicare coverage.

MEDICARE AND GENERAL MEDICAL NECESSITY

Non-MolDX Service Area Testing

Services areas which have **not** adopted MolDX guidelines include testing performed in the following states: FL, CO, NM, OK, TX, AR, LA, MS, DE, MD, NJ, PA, IL, MN, WI, CT, NY, ME, MA, NH, RI, and VT.

Testing Performed in Pennsylvania and Massachusetts

The local MAC for Pennsylvania is Novitas Solutions. Prior to 9/17/2014, Novitas had a limited-coverage LCD for circulating tumor cell (CTC) marker assays (L33232). However, Novitas retired this LCD as of 9/17/2014.

The local MAC for Massachusetts is National Government Services (NGS). NGS does not have, and does not appear to have ever had, a coverage policy (LCD or LCA) for ctDNA testing, and their LCD for circulating tumor cell (CTC) tests was retired in February 2016.

Only medically reasonable and necessary services or items which treat illness or injury are eligible for Medicare coverage, as outlined in *Title XVIII of the Social Security Act, §1862(a)(1)(A)*. MA organizations (MAOs) make medical necessity determinations based on coverage and benefit criteria, current standards of care, the member's unique personal medical history (e.g., diagnoses, conditions, functional status, co-morbidities, etc.), physician recommendations, and clinical notes, as well as involvement of a plan medical director, where appropriate. *(§ 422.101(c)(1))*

In addition:

"MA organizations may create publicly accessible internal coverage criteria that are based on current evidence in widely used treatment guidelines or clinical literature when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs. Current, widely-used treatment guidelines are those developed by organizations representing clinical medical specialties, and refers to guidelines for the treatment of specific diseases or conditions. Acceptable clinical literature includes large, randomized controlled trials or prospective cohort studies with clear results, published in a peer-reviewed journal, and specifically designed to answer the relevant clinical question, or large systematic reviews or meta-analyses summarizing the literature of the specific clinical question." *(§ 422.101(b)(6) and Medicare Managed Care Manual, Ch. 4, §90.5)*

The Company policy for *PHA Medicare Medical Policy Development and Application* (MP50) provides details regarding Medicare's definition of medical necessity and the hierarchy of Medicare references and resources during the development of medical policies, as well as the Plan's use of evidence-based processes for policy development.
Since there are not fully established coverage criteria for ctDNA or CTC tests in these service areas available in applicable Medicare statutes, regulations, NCDs or LCDs (for the service area in which the testing is being performed), then Company medical policy criteria will be applied. See the Medicare Coverage Criteria table above for more information regarding the use of internal coverage criteria when Medicare coverage criteria are not fully established.

REGULATORY STATUS

U.S. FOOD & DRUG ADMINISTRATION (FDA)

While clearance by the Food and Drug Administration (FDA) is a prerequisite for Medicare coverage, the 510(k) premarket clearance process does not in itself establish medical necessity. Medicare payment policy is determined by the interaction of numerous requirements, including but not limited to, the availability of a Medicare benefit category and other statutory requirements, coding and pricing guidelines, as well as national and local coverage determinations and clinical evidence.

BILLING GUIDELINES AND CODING

GENERAL

See associated local coverage articles (LCAs) for additional coding and billing guidance.

- LCA: Billing and Coding: MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (A58185)
- LCA: Billing and Coding: MolDX: Plasma-Based Genomic Profiling in Tumors (A58975)
- LCA: Billing and Coding: MolDX: Plasma-Based Genomic Profiling in Tumors (A58973)

CODES*		
CPT	0177U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-hyphen4,5-hyphenbisphosphate 3-hyphenkinase catalytic subunit alpha) gene analysis of 11

		gene variants utilizing plasma, reported as PIK3CA gene mutation status *(Used to report the Therascreen PIK3CA test, by QIAGEN Sciences [using **plasma**]; Maryland)* *For the Therascreen PIK3CA test by QIAGEN Sciences using **tumor tissue** [0155U], see the Medicare medical policy for Genetic and Molecular Testing)*
	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) *(Used for the The Resolution ctDx Lung™ test, by Resolution Bioscience, Inc.)*
	0229U	BCAT1 (Branched chain amino acid transaminase 1) and IKZF1 (IKAROS family zinc finger 1) (eg, colorectal cancer) promoter methylation analysis *(Used for the Colvera® test, by Clinical Genomics Pathology, Inc.)*
	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 *(FoundationOne Liquid CDx, by Foundation Medicine, Inc.; Massachusetts)*
	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 *(Guardant360® CDx, by Guardant Health, Inc.; Washington)*
	0285U	Oncology, response to radiation, cell-free DNA, quantitative branched chain DNA amplification, plasma, reported as a radiation toxicity score *(Used to report the RadTox™ cfDNA test, by DiaCarta Inc.)*
	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 *(Used to report the LungLB® test, by LungLife AI®)*
	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 number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden *(Used to report the Guardant360® test, by Guardant Health Inc.)*
	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 *(Used to report the HelioLiver™ Test, by Fulgent Genetics LLC and Helio Health Inc.)*
	0337U	Oncology (plasma cell disorders and myeloma), circulating plasma cell immunologic selection, identification, morphological characterization, and enumeration of plasma cells based on differential CD138, CD38, CD19, and CD45 protein biomarker expression, peripheral blood *(Used to report the CELLSEARCH® Circulating Multiple Myeloma Cell (CMMC) Test, by Menarini Silicon Biosystems Inc.)*
	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 *(Used*

		to report the CELLSEARCH® HER2 Circulating Tumor Cell (CTC–HER2) Test, by Menarini Silicon Biosystems Inc.)
	0342U	Oncology (pancreatic cancer), multiplex immunoassay of C5, C4, cystatin C, factor B, osteoprotegerin (OPG), gelsolin, IGFBP3, CA125 and multiplex electrochemiluminescent immunoassay (ECLIA) for CA19-9, serum, diagnostic algorithm reported qualitatively as positive, negative, or borderline *(Used to report the IMMray® PanCan–d test, by Immunovia Inc.)*
	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 *(Used to report the NavDx® test, by Naveris Inc.)*
	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 *(Used to report the ColoScape™ Colorectal Cancer Detection test by DiaCarta Clinical Lab)*
	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 *(Used to report the InVisionFirst®-Lung Liquid Biopsy by Inivata, Inc.)*
	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 *(Used to report the OncobiotaLUNG test by Micronoma™)*
	~~0397U~~	**TERMED 9/30/2023** ~~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 *(Used to report the Agilent Resolution ctDx FIRST test by Resolution Bioscience, Inc.)*~~
	0404U	Oncology (breast), semiquantitative measurement of thymidine kinase activity by immunoassay, serum, results reported as risk of disease progression *(Used to report the DiviTum®Tka test by Biovica Inc.)*
	0405U	Oncology (pancreatic), 59 methylation haplotype block markers, next-generation sequencing, plasma, reported as cancer signal detected or not detected *(Used to report the BTG Early Detection of Pancreatic Cancer test by Breakthrough Genomics)*
	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 *(Used to report the LiquidHALLMARK® test by Lucence Health, Inc.)*
	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 *(Used to report the Guardant360 Response™ test by Guardant Health, Inc.)*

	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 *(Used to report the Epic Sciences ctDNA Metastatic Breast Cancer Panel test by Epic Sciences, Inc.)*
	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) *(Used to report the ColonAiQ® test by Breakthrough Genomics)*
	81309	PIK3CA (phosphatidylinositol-hyphen4, 5-hyphenbiphosphate 3-hyphenkinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)
	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
	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
HCPCS	None	

***Coding Notes:**

- The code list above is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit. According to Medicare, "presence of a payment amount in the MPFS and the Medicare physician fee schedule database (MPFSDB) does not imply that CMS has determined that the service may be covered by Medicare." The issuance of a CPT or HCPCS code or the provision of a payment or fee amount by Medicare does **not** make a procedure medically reasonable or necessary or a covered benefit by Medicare. *(Medicare Claims Processing Manual, Chapter 23 – Fee Schedule Administration and Coding Requirements, §30 – Services Paid Under the Medicare Physician's Fee Schedule, A. Physician's Services)*
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Medicare Benefit Policy Manual, Chapter 15 – Covered Medical and Other Health Services, §80.1 – Clinical Laboratory Services. Last updated 11/19/2007. Available at: https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/bp102c15.pdf. Accessed 6/12/2024.
2. 42 CFR § 410.32(a). Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests. Available at: https://www.govinfo.gov/content/pkg/CFR-2011-title42-Vol2/pdf/CFR-2011-title42-vol2-sec410-32.pdf. Accessed 6/12/2024.
3. Centers for Medicare and Medicaid Services (CMS). Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §50.5 - Jurisdiction of Laboratory Claims. Last updated: 12/22/2014. Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c16.pdf. Accessed 6/12/2024.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
1/2023	Q1 2023 code updates (converted to new format 2/2023)
4/2023	Q2 2023 code update; corrected criteria applied to RadTox™ cfDNA
7/2023	Q3 2023 code update and annual review
10/2023	Q4 2023 code updates
1/2024	Q1 2024 code updates
2/2024	Interim update, added CPT code for FoundationOne Liquid CDx
7/2024	Q3 2024 code updates
8/2024	Annual review; update to policy format, but no change to criteria