MEDICAL POLICY	**Circulating Tumor Cell and DNA Assays For Cancer Management (Medicare Only)**
Effective Date: 8/1/2022  8/1/2022 Medical Officer Date	Medical Policy Number: 306 Medical Policy Committee Approved Date: 5/2021; 11/2021; 3/2022; 6/2022

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

Medicare Only

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.

MEDICARE POLICY CRITERIA

The following Centers for Medicare & Medicaid Service (CMS) guidelines should be utilized for medical necessity coverage determinations. Click the link provided in the table below to access applicable medical necessity criteria. All listed guidelines apply.

Notes:

- This policy does not address cell-free DNA tests (also known as circulating tumor DNA tests or liquid biopsies) for targeted therapies for non-small cell lung cancer. (See Cross References section below)

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 Tests – 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.)*

	See "Policy Guidelines" below for important information regarding the NCD 90.2
All Other Plasma Based (liquid biopsy) Testing	For the Guardant360 LDT® (0326U): • Local Coverage Article (LCA): Billing and Coding: Guardant360® (A58192) *(See separate row for the FDA approved CDx test)* For all other plasma-based (liquid biopsy) tests: • **Testing performed in NC, SC, AL, GA, VA, WV, AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA and NV:** LCD: MolDX: Plasma-Based Genomic Profiling in Solid Tumors (L38043)* **NOTES:** 1. LCD L38043 will be used until a corresponding LCD for each respective service area is effective and final. Once each service area's LCD is final, it will replace L38043 for that service area. 2. According to this LCD, "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.
	This list includes tests which are considered **not medically necessary**, based on Medicare guidelines (see *"Policy Guidelines"* below) and the above LCD(s). • LungLB® (LungLife AI® (Code 0317U; California) *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)
Tests Not Otherwise Addressed *Examples:* • *RadTox™ cfDNA test (DiaCarta Clinical Lab) (Code 0285U)*	Company medical policy for Circulating Tumor Cell and DNA Assays for Cancer Management (All Lines of Business Except Medicare) I. These services are considered not medically necessary for Medicare based on the Company medical policy. *Services deemed "investigational" are considered not medically necessary for Medicare Plan members. See Policy Guidelines below.*

POLICY GUIDELINES

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

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

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).*

Medicare and General Medical Necessity

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. In the absence of Medicare coverage policies (e.g., manual, national coverage determination [NCD], local coverage determination [LCD], article [LCA], etc.), Medicare regulatory guidelines do allow Medicare Advantage Organizations (MAOs) to make their own coverage determinations, as long as the MAO applies an objective, evidence-based process, based on authoritative evidence. *(Medicare Managed Care Manual, Ch. 4, §90.5)*

Following an evidence-based assessment of current peer-reviewed medical literature, the Company may consider certain medical services or technologies to be "investigational." The term "investigational" is not limited to devices or technologies which have not received the appropriate governmental regulatory approval (e.g., U.S. Food and Drug Administration [FDA]), but rather may also mean the procedure, device, or technology does not meet all of the Company's technology assessment criteria, as detailed within the Company policy for *Definition: Experimental/Investigational* (MP5).

For Medicare, 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)*. Thus, services which lack scientific evidence regarding safety and efficacy because they are investigational are "not medically reasonable or necessary" for Medicare Plan members. *(Medicare Claims Processing Manual, Ch. 23, §30 A)*

BILLING GUIDELINES

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)

CPT/HCPCS CODES

Medicare Only	
Prior Authorization Required	
0155U	PIK3CA (phosphatidylinositol-hyphen4,5-hyphenbisphosphate 3-hyphenkinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A, p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R, p.H1047Y)
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
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® tests, by Clinical Genomics Pathology, Inc.)*
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
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)
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
Not Covered	
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
Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then **prior-authorization is required.**	
81479	Unlisted Molecular Pathology

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to

determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

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.

MEDICAL POLICY CROSS REFERENCES

Pharmacy Policies

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