| MEDICAL POLICY | Circulating Tumor Cell and DNA Assays For Cancer Management (Medicare Only) |
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| **Effective Date: 4/1/2022**<br>  <br>4/1/2022<br>Medical Officer Date | Medical Policy Number: 306<br>Medical Policy Committee Approved Date: 5/2021; 11/2021; 3/2022 |

**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 |
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| *Next-generation sequencing assays performed on solid tumor cell-free DNA in plasma (i.e. liquid biopsies)*<br><br>**See "Policy Guidelines" for notes regarding Guardant360 test options.** | • For all FDA-approved or FDA-cleared tests: National Coverage Determination (NCD) for Next Generation Sequencing (NGS) (90.2)<br><br>***Note:** This NCD is limited to NGS *DNA* sequencing tests which are FDA-approved or cleared as a companion diagnostic (CDx) test **and** only when used for cancer-related purposes. For all other tests, including tests which are **not** FDA-approved or cleared as a CDx test, tests which have a specific LCD or LCA available, NGS *RNA* sequencing tests, tests performed for indications ***outside*** of their FDA-approved or -cleared intended use, or for tests related to *non*-cancer indications, see separate Medicare references below or separate Medicare policies.<br><br>• Testing performed in NC, SC, AL, GA, VA, KY, OH, WV, AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY, CA and NV: Local Coverage Determination (LCD): MolDX: Plasma-Based Genomic Profiling in Solid Tumors (L38043)* |

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| | *Since several Medicare contractors use MolDX guidance policies, the Palmetto 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.<br><br>The above LCD requires successful completion of a technical assessment (TA) by the MolDX Program contractor. 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®." Tests that do not have FDA-approval or clearance must be listed on the DEX™ Change Healthcare Registry website as a potentially covered test by MolDX for Medicare. If a test is not listed in this policy, further research may be required.<br><br>• Local Coverage Article (LCA): Billing and Coding: Guardant360® (A58214) *(Note, this is the laboratory developed test available as of May 2014, not the CDx test, which is FDA-approved)*<br>• LCD for MolDX: Phenotypic Biomarker Detection from Circulating Tumor Cells (L38645)<br><br>LungLB® (LungLife AI® (Code 0317U; California) is **not medically necessary** because it does not have the TA review required by the LCDs L38043 or L38645. |
| *PIK3CA Gene Tests* | Local Coverage Article: Billing and Coding: MolDX: PIK3CA Gene Tests (A55200) |

*In the absence of a Medicare coverage policy or guidance (e.g., manual, national coverage determination [NCD], local coverage determination [LCD] article [LCA], etc.), Medicare guidelines allow a Medicare Advantage Organization (MAO) to make coverage determinations, applying an objective, evidence-based process, based on authoritative evidence. (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5) Therefore, the commercial medical policy***, Circulating Tumor Cell and DNA Assays For Cancer Management (All Lines of Business Except Medicare)** *applies to the following services:*

- RadTox™ cfDNA test (DiaCarta Clinical Lab) (Code 0285U)

## POLICY GUIDELINES

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.

## 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 | |
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| **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) or IKZF1 (IKAROS family zinc finger 1) (eg, colorectal cancer) promoter methylation analysis |
| 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**<br>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

Medical Policies

- Circulating Tumor Cell and DNA Assays For Cancer Management (All Lines of Business Except Medicare)
- Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (All Lines of Business Except Medicare)
- Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only)
- Genetic Testing: Non-Covered Genetic Panel Tests (Medicare Only)
- Genetic Studies and Counseling

Pharmacy Policies

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