

Medicare Advantage Medical Policy



Circulating Tumor DNA and Circulating Tumor Cells for Selecting Targeted Therapy for Advanced Solid Cancers (Liquid Biopsy) – Medicare Advantage

Medicare Advantage Plan

- ☒ Medicare Plus BlueSM
- ☒ BCN AdvantageSM

UM Committee Approval Date: 1/28/2026

Effective Date: 2/28/2026

Description

Liquid biopsy refers to the analysis of circulating tumor DNA (ctDNA) or circulating tumor cells (CTCs) as methods of noninvasively characterizing tumors and tumor genome from the peripheral blood.

ctDNA refers to cell-free DNA fragments of tumor origin that are present in the bloodstream. These fragments can be detected and analyzed using various molecular techniques, including next-generation sequencing (NGS), polymerase chain reaction (PCR), and quantitative PCR (qPCR). ctDNA analysis can provide insights into actionable mutations, such as EGFR, KRAS, or BRAF, as well as genomic instability, including microsatellite instability (MSI) or DNA mismatch repair deficiency (dMMR).

CTCs are intact tumor cells that have detached from the primary tumor and circulate in the bloodstream. CTCs can be isolated and analyzed using various techniques, including immunomagnetic separation, microfluidics, and single-cell analysis. CTC analysis can provide insight into the tumor cells ability to metastasize and possible response to therapy.

Related Medical Coverage Policies

- Prostate Cancer Early Detection: Biomarkers Prior to Biopsy
 - Genetic Testing – Next-Generation Sequencing of Multiple Genes (Panel) for Solid and Hematolymphoid Malignant Conditions
 - Somatic Biomarker Testing (including Liquid Biopsy) for Targeted Treatment and Immunotherapy in Metastatic Colorectal Cancer (KRAS, NRAS, BRAF, MMR/MSI, HER2, and TMB)
 - Genetic Testing - Somatic Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment and Immunotherapy in Non-Small-Cell Lung Cancer (EGFR, ALK, BRAF, ROS1, RET, MET, KRAS, HER2, PD-L1, TMB)
 - Circulating Tumor DNA for Management of Non-Small-Cell Lung Cancer (Liquid Biopsy)
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Policy Guidelines

Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network of Michigan (BCN) adhere to guidance from the Centers for Medicare and Medicaid Services (CMS), including when performing organization determinations for Medicare Advantage plan members. CMS Medicare statutes, regulations, manuals, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and other sub-regulatory guidance provide the clinical guidelines for coverage determinations, payment integrity functions, and all other uses by CMS regulations. When CMS Medicare guidance is silent, incomplete, or insufficient, CMS permits BCBSM/BCN to utilize “internal coverage criteria”, such as independent criteria, health plan policy research, LCD/LCAs outside the services area or research from independent medical research repositories (i.e., Hayes) for coverage policies 42 CFR § 422.101. BCBSM/BCN internal medical coverage policies are developed and based on current evidence in widely accepted treatment guidelines or clinical literature; in addition, they address how clinical benefits may or may not outweigh member harm.

Clinical review follows guidance provided in the BCBSM Medicare Advantage Coverage Determination Hierarchy policy, which may be found at <https://www.bcbsm.com/providers/mpradmin/> by entering the policy name.

Coverage Guidance

To ensure consistency with coverage guidance, the Medicare statutes, regulations, coverage manuals, NCD, LCD, and LCA should be reviewed and applied first. BCBSM/BCN internal coverage criteria should only be applied when CMS guidance is silent, incomplete, or insufficient for a code.

Apart from durable medical equipment (DME), Medicare Administrative Contractor (MAC) jurisdiction for the purpose of clinical determination is based upon place of service. The place of service for laboratory testing is defined as the geographic location of the reference laboratory. Non-jurisdictional LCD/LCAs may not be utilized for a determination unless they have been specifically identified as internal coverage criteria by the policy. Alternatively, jurisdiction for DME MAC is determined by the member place of residence. Please see CMS Medicare Administrative Contractors (MAC) table for state MAC assignments below.

CMS Guidance	Additional Guidance
National Regulatory Guidance 42 CFR 405 subpart B - Medicare Coverage of Items and Services in Investigational Device Exemption (IDE) Studies For additional clinical trial information related to circulating tumor DNA for advanced solid cancers, please refer to https://clinicaltrials.gov National Coverage Determinations NCD: 90.2 – Next Generation Sequencing (NGS) NCD: 310.1 - Routine Costs in Clinical Trials Local Coverage Determinations WPS	BCBSM/BCN will follow CMS guidance as the primary source for coverage determinations. However, in instances where CMS guidance is silent, incomplete, or insufficient for a particular code, BCBSM/BCN internal coverage criteria will be applied to ensure consistent and informed decision-making. In such cases, please refer to the relevant BCBSM/BCN policy for guidance: <i>Circulating Tumor DNA and Circulating Tumor Cells for Selecting Targeted Therapy for Advanced Solid Cancers (Liquid Biopsy)</i> To access this policy, please visit the BCBS Michigan Medical Policy Router Search page at

L38168, A57935 – MolDX: Plasma-Based Genomic Profiling in Solid Tumors* L38158, A57858 – MolDX: Next Generation Sequencing for Solid Tumors* A55197 - Moldx: Targeted and Comprehensive Genomic Profile Testing in Cancer* L38684, A58211 – MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer* L38835 - MolDX: Minimal Residual Disease Testing for Cancer* A58468 – Billing and Coding: MolDX: Minimal Residual Disease Testing for Solid Tumor Cancers* L36807, A57772 – MolDX: Molecular Diagnostic Tests (MDT)* CGS L38065, A57917 – MolDX: Plasma-Based Genomic Profiling in Solid Tumors* L38067, A57870 – MolDX: Next-Generation Sequencing for Solid Tumors* L38586, A58065 – MolDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer* L38822 - MolDX: Minimal Residual Disease Testing for Cancer* A58434 – Billing and Coding: MolDX: Minimal Residual Disease Testing for Solid Tumor Cancers* L36021, A56973 - MolDX: Molecular Diagnostic Tests (MDT)* First Coast L34519, A57451 - Molecular Pathology Procedures A58918 - Billing and Coding: Molecular Pathology and Genetic Testing [Not an LCD reference model article] NGS L37810, A56867 – Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms L35000, A56199 - Molecular Pathology Procedures Noridian JE L39230, A58973 – MolDX: Plasma-Based Genomic Profiling in Solid Tumors* L38119, A57901 – MolDX: Next-Generation Sequencing for Solid Tumors* A55624 – Billing and Coding: MolDX: Targeted and Comprehensive Genomic Profile Testing in Cancer*	https://www.bcbsm.com/providers/mpradmin/ and enter the policy name in the search field.
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L38647, A58181 – MoIDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer*

L38814 - MoIDX: Minimal Residual Disease Testing for Cancer*

A58454 – Billing and Coding: MoIDX: Minimal Residual Disease Testing for Solid Tumor Cancers*

L35160, A57526 - MoIDX: Molecular Diagnostic Tests (MDT)*

Noridian JF

L39232, A58975 – MoIDX: Plasma-Based Genomic Profiling in Solid Tumors*

L38121, A57905 – MoIDX: Next-Generation Sequencing for Solid Tumors*

A56518 – Billing and Coding: MoIDX: Targeted and Comprehensive Genomic Profile Testing in Cancer*

L38649, A58181 – MoIDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer*

L38816 - MoIDX: Minimal Residual Disease Testing for Cancer*

A58456 – Billing and Coding: MoIDX: Minimal Residual Disease Testing for Solid Tumor Cancers*

L36256, A57527 - MoIDX: Molecular Diagnostic Tests (MDT)*

Novitas

L35396, A52986 – Biomarkers for Oncology

L35062, A56541 – Biomarkers Overview

A58917 – Billing and Coding: Molecular Pathology and Genetic Testing

Palmetto

L38043, A57867 – MoIDX: Plasma-Based Genomic Profiling in Solid Tumors*

L38045, A57831 – MoIDX: Next-Generation Sequencing for Solid Tumors*

A54795 – Billing and Coding: MoIDX: Targeted and Comprehensive Genomic Profile Testing in Cancer*

L38576, A58028 – MoIDX: Prognostic and Predictive Molecular Classifiers for Bladder Cancer*

L38779 - MoIDX: Minimal Residual Disease Testing for Cancer*

A58376 – Billing and Coding: MoIDX: Minimal Residual Disease Testing for Solid Tumor Cancers*

L35025, A56853 - MoIDX: Molecular Diagnostic Tests (MDT)*

Code	Description
81445	Solid organ neoplasm, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis
81455	Solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes, genomic sequence analysis panel, interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; DNA analysis or combined DNA and RNA analysis
81462	Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (e.g., 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 (e.g., 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 (e.g., plasma), interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants, microsatellite instability, tumor mutation burden, and rearrangements
86152	Cell enumeration using immunologic selection and identification in fluid specimen (e.g., circulating tumor cells in blood)
86153	Cell enumeration using immunologic selection and identification in fluid specimen (e.g., circulating tumor cells in blood); physician interpretation and report, when required
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 [FirstSightCRC™]
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 Dx,]
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,]
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 [Guardant360®]
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 [CELLSEARCH® CTC-HER2]
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 [Caris Assure™]
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 [Northstar Response™]

0487U	Oncology (solid tumor), cellfree 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 [Northstar Select™]
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 [CELLSEARCH® CTC-ER]
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 [CELLSEASRCH® CTC-PD-L1]
0530U	Oncology (pan-solid tumor), ctDNA, utilizing plasma, next generation sequencing (NGS) of 77 genes, 8 fusions, microsatellite instability, and tumor mutation burden, interpretative report for single-nucleotide variants, copy number alterations, with therapy association
0539U	Oncology (solid tumor), cell-free circulating tumor DNA (ctDNA), 152 genes, next-generation sequencing, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, copy number alterations, and microsatellite instability, using whole-blood samples, mutations with clinical actionability reported as actionable variant
0571U	Oncology (solid tumor), DNA (80 genes) and RNA (10 genes), by next-generation sequencing, plasma, including single nucleotide variants, insertions/deletions, copy number alterations, microsatellite instability, and fusions, reported as clinically actionable variants
0585U	Targeted genomic sequence analysis panel, solid organ neoplasm, circulating cell-free DNA (cfDNA) analysis from plasma of 521 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, and microsatellite instability, report shows identified mutations, including variants with clinical actionability

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* CMS MoIDX Program

The MoIDX Program, administered by Palmetto GBA, is a Medicare Molecular Diagnostic Program that aims to identify and establish coverage and reimbursement for molecular diagnostic tests. This program is implemented by several Medicare Administrative Contractors (MACs), including **WPS, CGS, Noridian, and Palmetto**.

The MoIDX Program evaluates genetic tests to determine their analytical and clinical validity (AV/CV) and clinical utility (CU), ensuring that each test meets Medicare criteria.

The program's coverage determinations are maintained in the DEX™ Diagnostic Exchange registry. Dex Diagnostic Exchange Registry Coverage Determinations:

1. **Not Covered:** Not covered tests in the Dex Registry have undergone a review of their clinical utility and analytical validity and have been determined to not meet the requirements for medical necessity under Section 1862(a)(1)(A) of the Social Security Act. As a result, they are not considered medically reasonable or necessary for Medicare coverage.
2. **No Determinations:** Tests that have not completed the required technical assessment (TA) review are, by default, also considered not medically reasonable or necessary for Medicare under Section 1862(a)(1)(A) until the review is completed. The MoIDX Program does not provide coverage for tests provided with dates of services prior to the effective date of approval.
3. **Covered:** Covered Tests in Dex Registry have completed the required TA review and have been determined to be medically reasonable and necessary for Medicare under Section 1862(a)(1)(A). However, coverage is not automatic and is subject to the following conditions:

- a. The test must meet the applicable criteria outlined in NCDs, LCDs, and LCAs; and
- b. The patient must exhibit signs or symptoms of a relevant disease or condition, making the test medically necessary for their care.

For specific coding and billing information on covered and excluded tests, please refer to the MoIDX website at <https://www.palmettogba.com/MoIDX>. This website provides up-to-date information on the program's coverage determinations and guidelines.

NOTE: Per § 2.3.3. of the Molecular Diagnostic Program [MoIDX®] Manual, the MoIDX Program does not provide coverage for tests that have not been reviewed and approved through the MoIDX process or for tests provided with dates of services prior to the effective date of approval. For additional information regarding what tests will fall into a Medicare benefit category or which tests are statutory excluded (e.g., predictive, prenatal, and carrier testing and tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law) please refer to <https://www.palmettogba.com/palmetto/moldxv2.nsf/DID/DPR5GEM991>

The above information is current as of the review date for this policy. However, the coverage issues and policies maintained by CMS are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document.

Please refer to the Medicare Coverage Database website at <https://www.cms.gov/medicare-coverage-database/search.aspx> for the most current applicable NCD, LCD, LCA, and CMS Online Manual System Transmittals.

CMS Medicare Administrative Contractors (MAC) Jurisdictions Guidance

Part A and Part B MAC Jurisdictions	
Wisconsin Physicians Service Insurance Corporation (WPS)	IA, IN, KS, MI, MO, NE
CGS Administrators, LLC	KY, OH
First Coast Service Options, Inc	FL, PR, US VI
National Government Services, Inc (NGS)	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI,
Noridian Healthcare Solutions, LLC, Jurisdiction JE	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
Noridian Healthcare Solutions, LLC, Jurisdiction JF	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
Novitas Solutions, Inc	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX,
Palmetto GBA	AL, GA, TN NC, SC, VA, WV
DME MAC Jurisdictions	
CGS Administrators, LLC, Jurisdictions JB and JC	AL, AR, CO, FL, GA, IL, IN, KY, LA, MI, MN, MS, NM, NC, OH, OK, Puerto Rico, SC, TN, TX, VA, Virgin Island, WI, WV
Noridian Healthcare Solutions, LLC, Jurisdictions JA and JD	AK, American Soamoa, AZ, CA, CT, DE, DC, Guam, HI, ID, IA, KS, MA, MD, ME, MO, MT, ND, NE, NH, NJ, NV, NY, Northern Mariana Islands, OR, PA, RI, SD, UT, VT, WA, WY

Important Reminder

BCBSM and BCN follow CMS Medicare coverage guidance to limit coverage to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member. Medicare Advantage

Medical Policies list the criteria BCBSM and BCN use to decide which medical services are considered “reasonable and necessary” when Medicare coverage rules are not fully developed, or as otherwise may be permitted by CMS Medicare regulations. Individual member benefit plan documents, such as the Evidence of Coverage and Annual Notice of Change, as well as applicable laws govern benefit coverage, including any inclusion, exclusion, and/or other restrictions.

Medicare Advantage Medical policies are created when permitted by CMS Medicare regulations, reviewed regularly, and may be revised periodically. BCBSM/BCN Medical Policies are proprietary and should not be copied or disseminated without the express, prior written approval of BCBSM. All providers are required to review applicable BCBSM reimbursement policies prior to claim submission and bill for covered services in accordance with those policies. Additionally, providers contracted with BCBSM or BCN’s Medicare Advantage network(s) should review the provider manual for any additional claim submission requirements. Providers not contracted with BCBSM or BCN’s Medicare Advantage network may be required to submit documentation to BCBSM, BCN, or its delegated entity supporting billed claims, including but not limited to applicable medical records.

Note: U.S. Food and Drug Administration (FDA) approval for a specific indication or the issuance of a CPT code is not sufficient for a procedure to be considered medically reasonable and necessary. Similarly, the presence of a procedure/device code or payment amount for the service in the Medicare fee schedule does not necessarily indicate coverage. If a service is deemed not reasonable and necessary, to treat illness or injury for any reason (including lack of safety and efficacy because it is an experimental procedure, etc.), the procedure is considered not covered.

Disclaimer: This medical policy is not an authorization, certification, explanation of benefits, or a contract for the services, devices, or drugs that is referenced in the medical policy. Medical policies do not constitute medical advice and do not guarantee any results or outcomes or guarantee payment. The medical policy is not intended to replace independent medical judgment for the treatment of individuals. Treating physicians and health care providers are solely responsible for determining what care to provide to their patients. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test, or procedure over another.

Pursuant to Section 1557 and Section 504, Blue Cross does not discriminate on the basis of race, color, national origin, age, disability, or sex (including sex characteristics, intersex traits; pregnancy or related conditions; sexual orientation; gender identity, and sex stereotypes). This includes our rules, benefit designs and medical policies.

BCBSM/BCN Medicare Advantage Policy History

Policy Effective Date	UM Committee Approval Date	Comments
08/17/2024	07/17/2024	Medicare Advantage policy established
10/17/2025	09/17/2025	MA policy foundational language updated. Adoption of JUMP policy updates.
2/28/2026	1/28/2026	Adoption of JUMP policy updates.