

Medicare Advantage Medical Policy



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Somatic Biomarker Testing (including Liquid Biopsy) for Targeted Treatment and Immunotherapy in Metastatic Colorectal Cancer (KRAS, NRAS, BRAF, MMR/MSI, HER2, and TMB) – Medicare Advantage

Medicare Advantage Plan

- ☒ Medicare Plus BlueSM
- ☒ BCN AdvantageSM

UM Committee Approval Date: 01/28/2026

Effective Date: 02/28/2026

Description

Somatic biomarker testing can help identify patients with metastatic colorectal cancer who may benefit from targeted therapies. Somatic testing analyzes genetic mutations that are acquired during a person's lifetime and are specific to the tumor cells. In metastatic colorectal cancer, somatic testing is used to identify genetic alterations that can inform treatment decisions. Relevant somatic biomarkers in metastatic colorectal cancer include RAS (KRAS and NRAS) mutations, BRAF V600E mutation, microsatellite instability (MSI), HER2 amplification, and TP53 mutations. Testing methods can include next-generation sequencing (NGS), polymerase chain reaction (PCR), and immunohistochemistry (IHC).

The results of germline and somatic biomarker testing can inform the use of targeted therapies in metastatic colorectal cancer, including anti-EGFR therapy, BRAF inhibitors, immunotherapy, and anti-HER2 therapy.

Related Medical Coverage Policies

- Genetic Testing-Molecular Analysis for Targeted Therapy of Non-Small-Cell Lung Cancer
- Circulating Tumor DNA and Circulating Tumor cells for Cancer Management (liquid biopsy)
- Genetic Testing-NGS Testing of Multiple Genes (Panel) to Identify Targeted Cancer Therapy
- Genetic Cancer Susceptibility Panels Using NGS
- GT-Somatic Biomarker Testing for Immune Checkpoint Inhibitor Therapy (BRAF, MSI/MMR, PD-L1, TMB)

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 Coverage Determinations NCD: 90.2 - Next Generation Sequencing NCD: 310.1 - Routine Costs in Clinical Trials For additional information related to clinical trials related to somatic biomarkers of colorectal cancer Please refer to this URL: https://clinicaltrials.gov	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.
Local Coverage Determinations and Articles WPS L36807, A57772 - MoIDX: Molecular Diagnostic Tests (MDT)* A55161- MoIDX: FDA-Approved BRAF Tests*	In such cases, please refer to the relevant BCBSM/BCN policy for guidance: <i>Somatic Biomarker Testing (including Liquid Biopsy) for Targeted Treatment and Immunotherapy in Metastatic Colorectal Cancer (KRAS, NRAS, BRAF, MMR/MSI, HER2, and TMB)</i> To access this policy, please visit the BCBSM Medical Policy Router Search page at

A55162 – MoIDX: FDA-Approved KRAS Tests* L36797, A57581 – MoIDX: NRAS Genetic Testing* L38168, A57936 – MoIDX: Plasma-Based Genomic Profiling in Solid Tumor* L38429, A57100 - MoIDX: Repeat Germline Testing* L39040, A58756 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer* CGS L36021, A56973 - MoIDX: Molecular Diagnostic Tests (MDT)* A54191- MoIDX: FDA-Approved BRAF Tests A54688 - MoIDX: FDA-Approved KRAS Tests A54200 MoIDX: theascreen® KRAS PCR Kit Guidelines L35442, A56998 – MoIDX: NRAS Genetic Testing L38065, A57917 – MoIDX: Plasma-Based Genomic Profiling in Solid Tumor* L39017, A58734 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer* L38288, A57141 - MoIDX: Repeat Germline Testing First Coast L34912, A57450 – Genetic Testing for Lynch Syndrome L39367, A59123 - Genetic Testing for Oncology L34519, A57451- Molecular Pathology Procedures A58918 - Molecular Pathology and Genetic Testing NGS L35000, A56199 - Molecular Pathology Procedures L37810, A56867 – Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms Noridian JE L35160, A57526 - MoIDX: Molecular Diagnostic Tests (MDT)* A54418- MoIDX: FDA-Approved BRAF Tests* A54498 - MoIDX: FDA-Approved KRAS Tests* A56103 – MoIDX: Microsatellite Instability High and Mismatch Repair Deficient Biomarker for Patients with Unresectable or Metastatic Solid Tumors* L36335, A57486 - MoIDX: NRAS Genetic Testing* L39230, A58973 – MoIDX: Plasma-Based Genomic Profiling in Solid Tumor* L38351, A57331 - MoIDX: Repeat Germline Testing* L38972, A58679 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer *	https://www.bcbsm.com/providers/mpradmin/ and enter the policy name in the search field.
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Noridian JF

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

A54420 - MoIDX: FDA-Approved BRAF Tests*

A54500 - MoIDX: FDA-Approved KRAS Tests*

A56104 – MoIDX: Microsatellite Instability High and Mismatch Repair Deficient Biomarker for Patients with Unresectable or Metastatic Solid Tumors*

L36339, A57487 – MoIDX: NRAS Genetic Testing*

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

L38353, A57332 - MoIDX: Repeat Germline Testing*

L38974, A58681 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer*

Novitas

L39365, A59125 - Genetic Testing for Oncology

L35062 - Biomarkers Overview

L35396, A52986 –Biomarkers for Oncology

A58917 - Molecular Pathology and Genetic Testing

Palmetto

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

A54018 - MoIDX: FDA-Approved BRAF Tests*

A54472 - MoIDX: FDA-Approved KRAS Tests*

A56072 – MoIDX: Microsatellite Instability High and Mismatch Repair Deficient Biomarker for Patients with Unresectable or Metastatic Solid Tumors*

L35073, A56962 – MoIDX: NRAS Genetic Testing*

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

L38966, A58652 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer*

L38274, A58017 - MoIDX: Repeat Germline Testing*

Code	Description
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (e.g., colon cancer, melanoma), gene analysis, V600 variant(s)
81275	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g., carcinoma) gene analysis, variants in codons 12 and 13
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146)
81301	Microsatellite instability analysis (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (e.g., BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed

81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)
81403	Molecular pathology procedure, Level 4 (e.g. analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons): Includes KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g. carcinoma), gene analysis, variant(s) in exon 2
81404	Molecular pathology procedure, Level 5 (e.g., analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis) ...Includes NRAS (neuroblastoma RAS viral oncogene homolog) (e.g., colorectal carcinoma), exon 1 and exon 2 sequences
88363	Examination and selection of retrieved archival (i.e., previously diagnosed) tissue(s) for molecular analysis (e.g., KRAS mutation al analysis).
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MET, MLL, NOTCH1, NPM1, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), 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
81456	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MET, MLL, NOTCH1, NPM1, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis
86152	Cell enumeration using immunologic selection and identification in fluid specimen (e.g., circulating tumor cells in blood); [Cellsearch® CTC, CellMax -CRC]
86153	Cell enumeration using immunologic selection and identification in fluid specimen (e.g., circulating tumor cells in blood); physician interpretation and report, when required
88363	Examination and selection of retrieved archival (i.e., previously diagnosed) tissue(s) for molecular analysis (e.g., KRAS mutation al analysis).
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden [FoundationOne CDx™ (F1CDx®) test, Foundation Medicine, Inc]
0111U	Oncology (colon cancer), targeted KRAS (codons 12, 13, and 61) and NRAS (codons 12, 13, and 61) gene analysis utilizing formalin-fixed paraffin-embedded tissue. [Praxis™ Extended RAS Panel, Illumina]
0239U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free DNA, analysis of 311 or more genes interrogation for sequencing variants, including substitutions, insertions, deletions, select rearrangements, and copy number variations [FoundationOne® Liquid CDx, Foundation Medicine, Inc]
0242U	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 [Guardant360® CDx, Guardant Health 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 [Guardant360®, Guardant Health, Inc]
0334U	Oncology (solid organ), targeted genomic sequence analysis, formalin-fixed paraffin-embedded (FFPE) tumor tissue, DNA analysis, 84 or more genes, interrogation for sequence variants, gene

	copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden [Guardant360 Tissue, Guardant Health, Inc]
0471U	Oncology (colorectal cancer), qualitative real-time PCR of 35 variants of KRAS and NRAS genes (exons 2, 3, 4), formalin-fixed paraffin-embedded (FFPE), predictive, identification of detected mutations [CRCdx® RAS Mutation Detection Kit, EntroGen, Inc]
0473U	Oncology (solid tumor), next-generation sequencing (NGS) of DNA from formalin-fixed paraffin-embedded (FFPE) tissue with comparative sequence analysis from a matched normal specimen (blood or saliva), 648 genes, interrogation for sequence variants, insertion and deletion alterations, copy number variants, rearrangements, microsatellite instability, and tumor-mutation burden [xT CDx, Tempus AI, Inc]
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. [LiquidHALLMARK®, Lucence Health, Inc]
0211U	Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association [MI Cancer Seek™ - NGS Analysis, Caris MPI d/b/a Caris Life Sciences]

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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 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
04/19/2025	03/19/20205	MA policy foundational language updated. Adoption of JUMP policy updates.
2/28/2026	1/28/2026	Adoption of JUMP policy updates.