

Medicare Advantage Medical Policy



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Genetic Testing – NGS of Multiple Genes (Panel) for Solid and Hematolymphoid Malignant Conditions – Medicare Advantage

Medicare Advantage Plan

☒ Medicare Plus BlueSM

☒ BCN AdvantageSM

UM Committee Approval Date: 1/28/2026

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Description

Next-generation sequencing is one of several methods that allow the sequencing of large stretches of DNA. Panel testing is potentially associated with greater efficiencies in the evaluation of genetic diseases. Panel testing with next-generation sequencing (NGS) involves evaluating sequence variants in multiple genes at one time. For solid tumors, NGS panel testing typically involves analyzing a predefined set of genes known to be associated with cancer. These panels can range from a few dozen to several hundred genes and may include tumor suppressor genes (e.g., TP53, PTEN, RB1), oncogenes (e.g., KRAS, BRAF, PIK3CA), genes involved in DNA repair (e.g., BRCA1, BRCA2, MLH1), and genes associated with specific tumor types (e.g., EGFR, HER2). For hematolymphoid malignancies, NGS panel testing typically focuses on genes involved in the development and progression of these cancers and may include genes involved in cell signaling and proliferation (e.g., JAK2, MPL), genes involved in DNA methylation and epigenetic regulation (e.g., DNMT3A and TET2), and genes associated with specific hematolymphoid malignancies (e.g., FLT3, JAK2).

Related Medical Coverage Policies

- Genetic Testing – BRAF Mutation in Selecting Melanoma Patients for Targeted Therapy Including Liquid Biopsy – Medicare Advantage
- Genetic Cancer Susceptibility Panels Using Next Generation Sequencing – Medicare Advantage
Circulating Tumor DNA and Circulating Tumor Cells for Selecting Targeted Therapy for Advanced Solid Cancers (Liquid Biopsy) - Medicare Advantage
- Genetic Testing – Molecular Markers in Fine Needle Aspirates (FNA) of the Thyroid – Medicare Advantage
- Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes – Medicare Advantage
- Genetic Testing Germline Genetic Testing for BRCA1, BRCA2, and PALB2 for Hereditary Breast/Ovarian Cancer Syndrome and Other High-Risk Cancers - Medicare Advantage

- Somatic Biomarker Testing (Including liquid biopsy) for targeted treatment in metastatic colorectal cancer (KRAS, NRAS, BRAF, NTRK and HER2) – Medicare Advantage
- 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) – Medicare Advantage

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 (NGS)	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 WPS	

L36807, A57772 - MolDX: Molecular Diagnostic Tests (MDT)*

L38158, A57858 - MolDX: Next-Generation Sequencing for Solid Tumors*

A55197 - MolDX: Targeted and Comprehensive Genomic Profile Testing in Cancer*

CGS

L36021, A56973 - MolDX: Molecular Diagnostic Tests (MDT)*

L38067, A57870 - MolDX: Next-Generation Sequencing for Solid Tumors*

First Coast

L34519, A57451 - Molecular Pathology Procedures

A58918 - Molecular Pathology and Genetic Testing [Not an LCD reference model article]

NGS

L35000, A56199 - Molecular Pathology Procedures

L37810, A56867- Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms

Noridian JE

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

L38119, A57901 - MolDX: Next-Generation Sequencing for Solid Tumors*

A55624 - MolDX: Targeted and Comprehensive Genomic Profile Testing in Cancer*

Noridian JF

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

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

A56518 - MolDX: Targeted and Comprehensive Genomic Profile Testing in Cancer*

Novitas

L35062, A56541 – Biomarkers Overview

L35396, A52986 – Biomarkers for Oncology

A58917 –Molecular Pathology and Genetic Testing

Palmetto

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

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

A54795 - MolDX: Targeted and Comprehensive Genomic Profile Testing in Cancer*

In such cases, please refer to the relevant BCBSM/BCN policy for guidance:

Genetic Testing – NGS of Multiple Genes (Panel) for Solid and Hematolymphoid Malignant Conditions

To access this policy, please visit the BCBS Michigan Medical Policy Router Search page at <https://www.bcbsm.com/providers/mpradmin/> and enter the policy name in the search field.

Code	Description
81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (i.e., detection of large gene rearrangements) [BRACAnalysis CDx, Myriad Genetics Laboratories, Inc]
81191	NTRK1 (neurotrophic receptor tyrosine kinase 1) (e.g., solid tumors) translocation analysis
81192	NTRK2 (neurotrophic receptor tyrosine kinase 2) (e.g., solid tumors) translocation analysis
81193	NTRK3 (neurotrophic receptor tyrosine kinase 3) (e.g., solid tumors) translocation analysis
81194	NTRK (neurotrophic receptor tyrosine kinase 1, 2, and 3) (e.g., solid tumors) translocation analysis
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (e.g., colon cancer, melanoma), gene analysis, V600 variant(s)
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
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
81449	Targeted genomic sequence analysis panel, solid organ neoplasm, 5-50 genes (e.g., ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, MET, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed; RNA analysis
81450	Hematolymphoid neoplasm or disorder, genomic sequence analysis panel, 5-50 genes, 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
81451	Hematolymphoid neoplasm or disorder, genomic sequence analysis panel, 5-50 genes, interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; 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 (includes DNA and RNA targeted genomic sequence3 analysis, combined method)
81456	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; RNA analysis
81457	Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, microsatellite instability
81458	Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, copy number variants and microsatellite instability
81459	Solid organ neoplasm, genomic sequence analysis panel, 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 code [BRACAnalysis CDx, Myriad Genetics Laboratories, Inc]
0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence or absence of variants and associated therapy(ies) to consider [Oncomine™ Dx Target Test, Thermo Fisher Scientific]

Code	Description
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), Foundation Medicine, Inc]
0048U	Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s) [MSK-IMPACT (Integrated Mutation Profiling of Actionable Cancer Targets), Memorial Sloan Kettering Cancer Center]
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score [myChoice® CDx, Myriad Genetics Laboratories, 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]
0244U	Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single-nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor-mutational burden and microsatellite instability, utilizing formalin-fixed paraffin-embedded tumor tissue [Oncotype MAP™ PanCancer Tissue Test, Paradigm Diagnostics, Inc]
0250U	Oncology (solid organ neoplasm), targeted genomic sequence DNA analysis of 505 genes, interrogation for somatic alterations (SNVs [single nucleotide variant], small insertions and deletions, one amplification, and four translocations), microsatellite instability and tumor-mutation burden [PGDx elio™ tissue complete, Personal Genome Diagnostics, 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]
0379U	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA (523 genes) and RNA (55 genes) by next-generation sequencing, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability, and tumor mutational burden [Solid Tumor Expanded Panel, Quest Diagnostics®]
0444U	Oncology (solid organ neoplasia), targeted genomic sequence analysis panel of 361 genes, interrogation for gene fusions, translocations, or other rearrangements, using DNA from formalin-fixed paraffin-embedded (FFPE) tumor tissue, report of clinically significant variant(s) [Aventa FusionPlus™, Aventa Genomics, LLC]
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

Code	Description
	deletion alterations, copy number variants, rearrangements, microsatellite instability, and tumor-mutation burden [xT CDx, Tempus AI, Inc]
0478U	Oncology (non-small cell lung cancer), DNA and RNA, digital PCR analysis of 9 genes (EGFR, KRAS, BRAF, ALK, ROS1, RET, NTRK 1/2/3, ERBB2, and MET) in formalin-fixed paraffin-embedded (FFPE) tissue, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, and reported as actionable detected variants for therapy selection [Aventa FusionPlus™, Aventa Genomics, LLC]
0523U	Oncology (solid tumor), DNA, qualitative, next-generation sequencing (NGS) of single nucleotide variants (SNV) and insertion/deletions in 22 genes utilizing formalin-fixed paraffin embedded tissue, reported as presence or absence of mutation(s), location of mutation(s), nucleotide change, and amino acid change [oncoReveal™ CDx, Pillar Biosciences, Inc]
0538U	Oncology (solid tumor), next generation targeted sequencing analysis, formalin-fixed paraffin embedded (FFPE) tumor tissue, DNA analysis of 600 genes, interrogation for single-nucleotide variants, insertions/deletions, gene rearrangements, and copy number alterations, microsatellite instability, tumor mutation burden, reported as actionable variant [PredicineATLAS™ Assay, Predicine Inc]
0543U	Oncology (solid tumor), next generation sequencing of DNA from formalin-fixed paraffin-embedded (FFPE) tissue of 517 genes, interrogation for single nucleotide variants, multi nucleotide variants, insertions and deletions from DNA, fusions in 24 genes and splice variants in 1 gene from RNA, and tumor mutation burden [TruSight™ Oncology Comprehensive, Illumina, Inc]
0586U	Oncology, mRNA, gene expression profiling of 216 genes (204 targeted and 12 housekeeping genes), RNA expression analysis, formalin fixed paraffin-embedded (FFPE) tissue, quantitative, reported as log2 ratio per gene [RNA Salah Targeted Expression Panel, Moffitt Cancer Center Advanced Diagnostics Laboratory, Laboratory Developed Test]
0592U	Oncology (hematolymphoid neoplasms), DNA, targeted genomic sequence of 417 genes, interrogation for gene fusions, translocations, rearrangements, utilizing formalin-fixed paraffin embedded (FFPE) tumor tissue, results report clinically significant variant(s) [Aventa Lymphoma, Aventa Genomics, LLC]

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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 MolDX 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 MolDX website at <https://www.palmettogba.com/MolDX>. 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 [MolDX®] Manual, the MolDX Program does not provide coverage for tests that have not been reviewed and approved through the MolDX 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

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
08/16/2025	07/16/2025	Annual Review: MA policy foundational language updated. Adoption of JUMP policy updates.
2/28/2026	1/28/2026	Annual Review: Reformatted and updated guidance and code tables. Adoption of JUMP policy updates.