

Medicare Advantage Medical Policy



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Genetic Cancer Susceptibility Panels Using Next Generation Sequencing – Medicare Advantage

Medicare Advantage Plan

☒ Medicare Plus BlueSM

☒ BCN AdvantageSM

UM Committee Approval Date: 11/26/2025

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Description

Genetic cancer susceptibility panels using Next Generation Sequencing (NGS) are a type of genetic testing that analyzes multiple genes associated with an increased risk of developing certain types of cancer. This testing is designed to screen for individuals who may be at higher risk of developing cancer due to inherited genetic mutations. NGS is a high-throughput technology that allows for the simultaneous analysis of multiple genes and entire genomes. It enables the rapid sequencing of large amounts of DNA, providing a comprehensive view of an individual's genetic code. NGS is particularly useful for identifying genetic mutations that may be associated with an increased risk of cancer.

Related Medical Coverage Policies

- GT-BCR-ABL1 in CML and AML
 - GT-BRAF for Melanoma Targeted Therapy
 - GT-Circulating DNA Colon CA Recurrence
 - GT-NGS for Assessment of Measurable Residual-Hematological
 - GT-NGS of Multiple Genes Panel for Solid and Hematolymphoid Malignant Conditions
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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.

Code	Description	NCD/LCD/LCA	Additional Guidance
81201	APC (adenomatous polyposis coli) (e.g., familial adenomatous polyposis [FAP], attenuated FAP) gene analysis; full gene sequence	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. In such cases, please refer to the relevant BCBSM/BCN policy for guidance: <i>Genetic Cancer Susceptibility Panels Using Next Generation Sequencing</i> 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.
81202	APC (adenomatous polyposis coli) (e.g., familial adenomatous polyposis [FAP], attenuated FAP) gene analysis; known familial variants	Local Coverage Determinations WPS L36807, A57772 - MoIDX: Molecular Diagnostic Tests (MDT)* A55197 – Targeted and Comprehensive Genomic Profile Testing in Cancer	
81203	APC (adenomatous polyposis coli) (e.g., familial adenomatous polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants	A55161 - MoIDX: FDA-Approved BRAF Testing* A55206 – MoIDX: Sept9 Gene Test L39040, A58756 - MoIDX: Lab-Developed Tests for Inherited Cancer	
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase)		

Code	Description	NCD/LCD/LCA	Additional Guidance
	(e.g., colon cancer, melanoma), gene analysis, V600 variant(s)	Syndromes in Patients with Cancer*	
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis.	CGS L36021, A56973 - MoIDX: Molecular Diagnostic Tests (MDT)* A54901 –Targeted and Comprehensive Genomic Profile Testing in Cancer A54191 –MoIDX: FDA-Approved BRAF Testing* A54300 –MoIDX: Sept9 Gene Test	
81292	MLH1 (MutL Homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, lynch syndrome) gene analysis; full sequence analysis	L39017, A58374 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer* First Coast L34519, A57451 - Molecular Pathology Procedures A58918 - Molecular Pathology and Genetic Testing [Not an LCD reference model article] L34912, A57450 – Genetic Testing for Lynch Syndrome (e.g., MLH1, MSH2, MSH6, PMS2)	
81293	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants	NGS L35000, A56199 - Molecular Pathology Procedures L37810, A56867 – Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms	
81294	MLH1 (MutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	Noridian JE L35160, A57526 - MoIDX: Molecular Diagnostic Tests (MDT)* A54418 –MoIDX: FDA-Approved BRAF Testing* A55623 –MoIDX: SEPT9 Gene Test A55624 –Targeted and Comprehensive Genomic Profile Testing in Cancer	
81295	MSH2 (MutS homolog 2, Colon Cancer, Nonpolyposis Type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis		
81296	MSH2 (MutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene		

Code	Description	NCD/LCD/LCA	Additional Guidance
	analysis; known familial variants	L38972, A58679 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer*	
81297	MSH2 (MutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	Noridian JF L36256, A57527 - MoIDX: Molecular Diagnostic Tests (MDT)* A54420 –MoIDX: FDA-Approved BRAF Testing* A55628 –MoIDX: SEPT9 Gene Test	
81298	MSH6 (MutS homolog 6 [e. Coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	A56518 –Targeted and Comprehensive Genomic Profile Testing in Cancer L38974, A58681 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer*	
81299	MSH6 (MutS homolog 6 [e. Coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants	Novitas L35062, A56541 – Biomarkers Overview A58917 – Molecular Pathology and Genetic Testing	
81300	MSH6 (MutS homolog 6 [e. Coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	Palmetto L36256, A57527 - MoIDX: Molecular Diagnostic Tests (MDT)* A54018 –MoIDX: FDA-Approved BRAF Testing* A53702 –MoIDX: SEPT9 Gene Test	
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	L38966, A58652 - MoIDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer*	
81307	PALB2 (partner and localizer of BRCA2) (e.g., breast and pancreatic cancer) gene analysis; full gene sequence		
81308	PALB2 (partner and localizer of BRCA2) (e.g., breast and pancreatic cancer) gene		

Code	Description	NCD/LCD/LCA	Additional Guidance
	analysis; known familial variant		
81317	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		
81318	PMS2 (postmeiotic segregation increased 2 [s. Cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis		
81319	PMS2 (postmeiotic segregation increased 2 [s. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants		
81327	SEPT9 (Septin9) (e.g., colorectal cancer) methylation analysis		
81401	PMS2 (postmeiotic segregation increased 2 [s. cerevisiae]) (e.g., Hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants		
81403	Molecular pathology procedure, Level 2 (e.g., 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic variant disorder/triplet repeat); includes MUTYH (mutY homolog [E. coli]) (e.g., MYH-associated polyposis)		

Code	Description	NCD/LCD/LCA	Additional Guidance
81406	Molecular pathology procedure, Level 7 (e.g., analysis of 11-25 exons by DNA sequence analysis, variant scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia); includes MUTYH (mutY homolog [E. coli]) (e.g., MYH-associated polyposis),		
81435	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, 5 or more genes, interrogation for sequence variants and copy number variants		
81437	Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, 5 or more genes, interrogation for sequence variants and copy number variants		
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, 5-50 genes (e.g., ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combine DNA and RNA analysis.		

Code	Description	NCD/LCD/LCA	Additional Guidance
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, 5-50 genes (e.g., BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), 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.		
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed; DNA analysis or combined DNA and RNA analysis.		
81479	Unlisted molecular pathology procedure		
0101U	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatous polyposis), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance		

Code	Description	NCD/LCD/LCA	Additional Guidance
	when indicated (15 genes [sequencing and deletion/duplication], EPCAM and GREM1 [deletion/duplication only])		
0238U	Oncology (Lynch syndrome), genomic DNA sequence analysis of MLH1, MSH2, MSH6, PMS2, and EPCAM, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions [Genomic Unity® Lynch Syndrome Analysis]		
0333U	Oncology (liver), surveillance for hepatocellular carcinoma (HCC) in high-risk patients, analysis of methylation patterns on circulating cell-free DNA (cfDNA) plus measurement of serum of AFP/AFP-L3 and oncoprotein des-gamma-carboxy-prothrombin (DCP), algorithm reported as normal or abnormal result. [HelioLiver™ Test]		

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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
12/26/2025	11/26/2025	MA policy foundational language updated. Adoption of JUMP policy updates.

