

Medicare Advantage Medical Policy



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Nontraditional Biomarkers in Risk Assessment and Management of Cardiovascular Disease– Medicare Advantage

Medicare Advantage Plan

☒ Medicare Plus BlueSM

☒ BCN AdvantageSM

UM Committee Approval Date: 11/26/2025

Effective Date: 12/26/2025

Description

Numerous lipids and nonlipid biomarkers have been proposed as potential risk markers for cardiovascular disease (CVD). The biomarkers that have the most evidence in support of their use in clinical care include apolipoprotein B (apo B), apolipoprotein A1 (apo A1), apolipoprotein E (apo E), B-type natriuretic peptide, cystatin C, fibrinogen, high-density lipoprotein (HDL) subclass, leptin, low-density lipoprotein (LDL) subclass, lipoprotein(a), high sensitivity C-reactive protein (hs-CRP), and genetic biomarkers. These biomarkers have been studied as an alternative or addition to standard lipid panels for risk stratification in CVD or as treatment targets for lipid-lowering therapy.

Related Medical Coverage Policies

- Measurement of Lipoprotein-associated Phospholipase A₂ (Lp-PLA₂) and Secretory Type II Phospholipase A₂ (sPLA₂-IIA) in the Assessment of Cardiovascular Risk
- Myeloperoxidase (MPO) Immunoassay for Cardiac Disease Risk

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	CMS Guidance	Additional Guidance
81401	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 mutation disorder/triplet repeat) *Includes APOB (apolipoprotein B) (e.g., familial hypercholesterolemia type B), common variants (e.g., R3500Q, R3500W)	National Coverage Determinations 190.23 Lipid Testing Local Coverage Determinations and Articles WPS L36523, A57559 – MolDX*: Biomarkers in Cardiovascular Risk Assessment L36807, A57772 – MolDX*: Molecular Diagnostic Tests (MDT) A59700 – MolDx*: Defining Panel Services in MolDx* [Not an LCD reference article]	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>Nontraditional Biomarkers in Risk Assessment and Management of Cardiovascular Disease</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.
81405	Molecular pathology procedure, Level 6* (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)	CGS L36139, A57386 – MolDX*: Biomarkers in Cardiovascular Risk L37598, A56988 - Cystatin C Measurement	

Code	Description	CMS Guidance	Additional Guidance
	Includes full gene sequence <i>LDLR</i> (low density lipoprotein receptor)	L36021, A56973 – MolDX: Molecular Diagnostic Tests (MDT) A59698 – MolDX*: Defining Panel Services in MolDX* [Not an LCD reference article]	
81406	Molecular pathology procedure, Level 7 (e.g., analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) *Includes <i>PCSK9</i>	First Coast L37561, A57682 - Cystatin C Measurement L33943, A56425 - B-type Natriuretic Peptide (BNP) Testing L33267, A57649 - B-Type Natriuretic Peptide (BNP) L33908, A57803 - High Sensitivity C-Reactive Protein (hsCRP)	
82172	Apolipoprotein, each	L39084, A58797 - Genetic Testing for Cardiovascular Disease	
83695	Lipoprotein(a)	L34519, A57451 - Molecular Pathology Procedures	
84999	Unlisted chemistry procedure (may be used for <i>ARH</i> adaptor protein testing)		
86141	C-reactive protein; high sensitivity (hsCRP)	NGS L33573, A56826 - B-type Natriuretic Peptide (BNP) Testing	
82397	Chemiluminescent assay (may be used for leptin testing)	L35000, A56199 - Molecular Pathology Procedures	
82610	Cystatin C		
82664	Electrophoretic technique, not elsewhere specified (may be used for HDL subclass)	Noridian JE L36358, A57037 – MolDX*: Biomarkers in Cardiovascular Risk	
83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified (may be used for leptin testing)	L37616, A57643 - Lab: Cystatin C Measurement L35526, A57083 - B-type Natriuretic Peptide (BNP) Testing L35160, A57526 – MolDX*: Molecular Diagnostic Tests (MDT)	
83700	Lipoprotein, blood; electrophoretic separation and quantitation	A59685 – MolDx*: Defining Panel Services in MolDx* [Not an LCD reference article]	

Code	Description	CMS Guidance	Additional Guidance
83701	Lipoprotein, blood; high resolution fractionation and quantitation of lipoproteins including lipoprotein subclasses when performed (e.g., electrophoresis, ultracentrifugation)	Noridian JF L36362, A57055 – MolDX*: Biomarkers in Cardiovascular Risk Assessment L37618, A57644 - Cystatin C Measurement L34038, A57084 - B-type Natriuretic Peptide (BNP) Testing	
83704	Lipoprotein, blood; quantitation of lipoprotein particle numbers and lipoprotein particle subclasses (e.g., by nuclear magnetic resonance spectroscopy)	L36256, A57527 – MolDX*: Molecular Diagnostic Tests (MDT) A59687 – MolDx*: Defining Panel Services in MolDx* [Not an LCD reference article]	
83718	Lipoprotein, direct measurement; high density cholesterol (HDL-C)	Novitas L39082, A58795 - Genetic Testing for Cardiovascular Disease	
83719	Lipoprotein, direct measurement; VLDL cholesterol	L34911, A56416 - Assays for Vitamins and Metabolic Function	
83721	Lipoprotein, direct measurement; LDL cholesterol	L34856, A56643 - C-Reactive Protein High Sensitivity Testing (hsCRP)	
83722	Lipoprotein, direct measurement; small dense LDL cholesterol	L35062, A56541 - Biomarker Overview	
83880	Natriuretic peptide	Palmetto L36129, A56943 – MolDX*: Biomarkers in Cardiovascular Risk Assessment	
84181	Protein; Western Blot, with interpretation and report, blood or other body fluid (may be used for APOE phenotyping or genotyping)	L37581, A56853 - Lab: Cystatin C Measurement L33422, A56565 - Brain Natriuretic Peptide (BNP) Level	
85384	Fibrinogen; activity	L35025, A56853 – MolDX*: Molecular Diagnostic Tests (MDT)	
85385	Fibrinogen; antigen		
0052U	Lipoprotein, blood, high resolution fractionation and quantitation of lipoproteins, including all five major lipoprotein classes and subclasses of HDL, LDL, and VLDL by vertical auto profile	A59678 – MolDx*: Defining Panel Services in MolDx* [Not an LCD reference article]	

Code	Description	CMS Guidance	Additional Guidance
	ultracentrifugation (VAP Cholesterol Test)		

CPT® codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

HCPCS® codes, descriptions and materials are copyrighted by Centers for Medicare and Medicaid Services (CMS).

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

