

Clinical Policy: Cardiac Risk Assessment Laboratory Tests

Reference Number: CA.CP.MP.203

Effective Date: 10/05

Last Review Date: 10/20

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

This policy describes the medical necessity requirements for cardiac risk assessment laboratory blood tests. They are proposed to help to determine the risk for coronary artery disease (CAD), myocardial infarction (MI), plus other cardiac conditions and guide the individual's treatment.

Policy/Criteria

- I. It is the policy of California Health & Wellness that for following tests are medically necessary when the indications are met:
 - A. High-sensitivity C-reactive protein (hs-CRP) testing for the assessment of CAD when the member has undergone previous noninvasive tests for cardiac risk stratification and been found to be at intermediate risk, as evidenced by meeting all of the following:
 - i. LDL cholesterol levels between 100 to 130 mg/dL;
 - ii. Patient has ≥ 2 coronary heart disease (CHD) major risk factors, such as:
 - iii. Hypertension (BP ≥ 140 mmHg or on an antihypertensive medication),
 - iv. Low HDL cholesterol (< 40 mg/dL),
 - v. Diabetes,
 - vi. Family history of premature CHD in male first degree relative < 55 years; CHD in female first degree relative < 65 years,
 - vii. Man ≥ 45 years or woman ≥ 55 years,
 - viii. Current cigarette smoking;
 - ix. Global risk assessment using Framingham point scoring reveals a 10 to 20% risk of CHD per 10 years.
 - B. Apolipoprotein B in high risk individuals to assess if additional intense interventions are necessary when LDL cholesterol goals are reached.
- II. It is the policy of California Health & Wellness that any of the following tests are **investigational** to assess cardiac risk because the medical literature is inconclusive regarding the utility of these tests for screening, diagnosis or management of CHD:
 - A. hs-CRP testing for members at high-risk for CAD,
 - B. hs-CRP as a screening test for the general population or for monitoring response to therapy,
 - C. Complete profiles of cardiac risk,
 - D. Apolipoprotein A-I,
 - E. Apolipoprotein B for the general population,
 - F. Apolipoprotein E,
 - G. Lipoprotein remnants: intermediate density lipoproteins and small density lipoproteins (NMR LipoProfile),
 - H. High density lipoprotein subclasses (LpAI, LpAI/AII and/or HDL3 and HDL2),

Cardiac Risk Assessment Laboratory Tests

- I. Low density lipoprotein subclasses (small and large LDL particles) Lipoprotein(a) enzyme immunoassay,
- J. Angiotensin gene (AGT) (CardiaRisk)
- K. Fibrinogen,
- L. Lipoprotein-associated phospholipase A2 (Lp-PLA2) (PLAC), secretory phospholipase A2 (sPLA2-IIA),
- M. Noninvasive measurements of arterial elasticity by means of blood pressure waveforms (e.g., HDI PulseWave, CVProfilor),
- N. Post-challenge insulin, high,
- O. Iron levels,
- P. Serum uric acid,
- Q. Vertical auto profile: cholesterol test,
- R. Corus CAD gene expression testing (unless otherwise specified)
- S. Measurement of B-type natriuretic peptides,
- T. Carotid intima-media thickness (CIMT)

Background

CAD develops when the coronary arteries become damaged or diseased with plaque development. Myocardial ischemia occurs when blood flow to the heart is reduced, preventing it from receiving enough oxygen. This reduced blood flow is usually the result of a partial or complete blockage of the coronary arteries. This condition may be chronic, narrowing of the coronary artery over time and limiting of the blood supply to part of the muscle; or it can be acute, resulting from a sudden rupture of a plaque and formation of a thrombus.

CHD is the most common form of heart disease affecting seven million Americans. It could lead to a MI or other cardiac issues and is the result of CAD, which can begin earlier in an individual's life. Preventive measures are thought to delay the progression of CAD. Therefore, it is imperative to understand not only how to diagnose heart disease but also how to stratify its risk, an important factor in treatment decision making in patients with CAD. Once the initial diagnosis has been made, various cardiac tests can be used to obtain pertinent information about risk level and the appropriateness of medical versus more invasive treatments.

Biomarkers of CVD have been identified and evaluated as potential adjuncts to standard risk assessment strategies. For CHD, biomarkers must reflect the underlying biology of the vessel walls and the atherosclerotic process. Various markers include hs-CRP, homocysteine, and Lp-PLA2, which have been investigated as a tool for determining the risk of CVD in apparently healthy and asymptomatic individuals, thereby presenting the opportunity for targeted preventive efforts based on an individual's predicted risk profile.⁴

Hs-CRP is a laboratory test developed to evaluate a patient's risk of MI or other heart conditions. Studies suggest that hs-CRP is useful in detecting the small amounts of CRP in patients with atherosclerosis. Current data suggest that the addition of hs-CRP to standard lipid screening can improve the ability to detect absolute coronary risk. This is a critical issue because one-half of all MIs and strokes occur among individuals without overt hyperlipidemia. In addition, it was

Cardiac Risk Assessment Laboratory Tests

theorized that risk assessment based on hs-CRP levels might provide a superior prediction of response to statin therapy.⁷

Several meta-analyses, reviews and clinical studies have been published assessing the association of lipoprotein with CVD risk and events. Although consistently strong associations have been found between levels of lipoproteins and adverse cardiac health outcomes, evidence presented on the clinical utility of these measures continues to be inconsistent, conflicting and thus inconclusive. Clinical studies are ongoing to further assess and define the role and clinical utility of lipoprotein testing in CVD risk assessment, treatment and management.^{2 5 11}

Guidelines from the ACC and the ADA recommend the use of apoB in persons at elevated cardiometabolic risk to assess whether additional intense interventions are necessary when LDL cholesterol goals are reached (Brunzell et al, 2008). According to these guidelines, high-risk persons are those with known CVD, diabetes, or multiple CVD risk factors (i.e., smoking, hypertension, family history of premature CVD). The American Association of Clinical Chemistry has issued similar recommendations regarding the use of apoB (Contois et al, 2009). Guidelines from the American Association of Clinical Endocrinologists (2012) recommend apo B measurements to assess the success of LDL-C-lowering therapy. The guidelines note that LDL particle number as reflected by apo B is a more potent measure of cardiovascular disease (CVD) risk than LDL-C and LDL particle size (e.g., small, dense LDL).

The clinical evidence is insufficient to show an added benefit of CIMT testing beyond traditional lipid risk assessment. There is inadequate clinical evidence from prospective studies that the use of this technology alters patient management and improves clinical outcomes. Additional research involving larger, well-designed studies is needed to establish the role of arterial compliance in the early identification, prevention and management of CVD.

American Heart Association

High-sensitivity C-reactive protein (hsCRP) and coronary artery calcium (CAC) are the leading novel markers of cardiovascular risk and are most commonly suggested for use in a tailored treatment approach.

American College of Cardiology Foundation (ACCF) and American Heart Association (AHA).

In 2019, the American College of Cardiology (ACC) and American Heart Association (AHA) issued a joint statement on the primary prevention of cardiovascular disease which states regarding elevated Lp(a) “a relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥ 50 mg/dL or ≥ 125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).” The guideline further states regarding elevated apo B (≥ 130 mg/dL) that “a relative indication for its measurement would be triglyceride ≥ 200 mg/dL. A level ≥ 130 mg/dL corresponds to an LDL-C > 160 mg/dL and constitutes a risk-enhancing factor.” Lipoprotein-associated phospholipase A2 (Lp-PLA2) testing was not mentioned in the above 2019 guideline, which was a change from 2010 guidelines. In their prior guideline, Lp-PLA2 was given an IIb recommendation for assessing cardiovascular risk in intermediate-risk asymptomatic adults.

National Institute of Health Care Excellence (NICE)

Cardiac Risk Assessment Laboratory Tests

NICE has guidelines on ‘Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease’. However, these guidelines do not mention the laboratory testing for cardiac risks.

U.S. Preventive Services Task Force (USPSTF 2018)

- USPSTF recommends against screening for asymptomatic carotid artery stenosis in the general adult population. (D recommendation).
- The USPSTF also concluded that the evidence is insufficient to assess the balance of benefits and harms of using nontraditional risk factors, such as CIMT to screen asymptomatic men and women with no history of CHD to prevent CHD events.
- The U.S. Preventive Services Task Force (USPSTF) concluded that the evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors, such as lipoprotein(a), to screen asymptomatic men and women with no history of CHD to prevent CHD events
- The USPSTF notes that the current evidence is insufficient to assess the balance of benefits and harms of adding the ankle-index (ABI), high-sensitivity C-reactive protein (hsCRP) level, or coronary artery calcium (CAC) score to traditional risk assessment for cardiovascular disease (CVD) in asymptomatic adults to prevent CVD events

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2015, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	Description
82172	Apolipoprotein, each
83695	Lipoprotein (a)
83698	Lipoprotein-associated phospholipase A2 (Lp-PLA2)
83700	Lipoprotein, Blood; Electrophoretic Separation And Quantitation
83701	Lipoprotein, Blood; High Resolution Fractionation And Quantitation Of Lipoproteins Including Lipoprotein Subclasses When Performed (Eg, Electrophoresis, Ultracentrifugation)
83704	Lipoprotein, Blood; Quantitation Of Lipoprotein Particle Numbers And Lipoprotein Particle Subclasses (Eg, By Nuclear Magnetic Resonance Spectroscopy)
83718	Lipoprotein, direct measurement; high density cholesterol (HDL cholesterol)
83721	LDL cholesterol
83722	Lipoprotein, direct measurement; small dense LDL cholesterol

Cardiac Risk Assessment Laboratory Tests

CPT® Codes	Description
83695	Lipoprotein (a) enzyme immunoassay
83698	Lipoprotein-associated phospholipase A2 (Lp-PLA2)
83880	Natriuretic peptide
84999	Unlisted chemistry procedure
86140	C-reactive protein
86141	C-reactive protein; high sensitivity (hsCRP)
93799	Unlisted cardiovascular service or procedure
0126T	Common carotid intima-media thickness (IMT) study for evaluation of atherosclerotic burden or coronary heart disease risk factor assessment

HCPCS Codes	Description
N/A	

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

ICD-10-CM Code	Description
E10.9	Type I diabetes mellitus without complication
E11.9	Type II diabetes mellitus without complication
E78.0- E78.89	Disorders of lipoprotein metabolism and other lipidemias
I24.0	Acute coronary thrombosis not resulting in MI
I24.8	Other forms of acute ischemic heart disease
I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
I25.110- I25.119	Atherosclerotic heart disease of native coronary artery with angina pectoris
I25.810- I25.9	Other forms of chronic ischemic heart disease
Z13.1	Encounter for screening for diabetes mellitus
Z13.220	Encounter for screening for lipid disorders
Z13.6	Encounter for screening for cardiovascular disorders

Reviews, Revisions, and Approvals	Date	Approval Date
Policy adopted from Health Net NMP 203, Cardiac Risk Assessment Laboratory Tests	10/16	10/16
Updated references, no changes	10/17	10/17
Added secretory phospholipase A2 (sPLA2-IIA) and Carotid intima-media thickness (CIMT) to investigational section. Updated references and background information	10/18	10/18

Cardiac Risk Assessment Laboratory Tests

Reviews, Revisions, and Approvals	Date	Approval Date
Added Apolipoprotein B as medically necessary for high risk individuals but not for general population	10/19	10/19
Removed homocysteine as there is a separate Centene Clinical Policy		
Updated society and college recommendations, codes and references	10/20	10/20

References

1. AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices, Cole TG, Contois JH, Csako G, et al. Association of apolipoprotein B and nuclear magnetic resonance spectroscopy-derived LDL particle number with outcomes in 25 clinical studies: assessment by the AACC Lipoprotein and Vascular Diseases Division Working Group on Best Practices. *Clin Chem*. 2013;59(5):752-770.
2. American College of Cardiology Foundation (ACCF) and American Heart Association (AHA). 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: Executive Summary. *Journal of the American College of Cardiology*. Available at: <http://content.onlinejacc.org/>
3. Berglund L, Brunzell JD, Goldberg AC, et al. Evaluation and treatment of hypertriglyceridemia: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2012;97(9):2969-2989.
4. Brunzell JD, Davidson M, Furberg CD, et al. Lipoprotein management in patients with cardiometabolic risk. Consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes Care*. 2008;31(4):811-822
5. Contois JH, McConnell JP, Sethi AA, et al.; AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. Apolipoprotein B and cardiovascular disease risk: Position statement from the AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. *Clin Chem*. 2009;55(3):407-419.
6. Garg PK, McClelland L, Jenny NS, et al. Lipoprotein-associated phospholipase A2 and risk of incident cardiovascular disease in a multi-ethnic cohort: The multi ethnic study of atherosclerosis. *Atherosclerosis*. 2015 Jul;241(1):176-82. doi: 10.1016/j.atherosclerosis.2015.05.006. Epub 2015 May 16.
7. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(25 Suppl 2):S49-S73.
8. Hayes GTE Overview. Corus CAD. September 2014. Updated September 12, 2016.
9. Hayes Health Technology Directory. Lipoprotein-Associated Phospholipase Testing for Coronary Heart Disease Risk Assessment in Healthy or Asymptomatic Adults. Updated October 7, 2015. Archived January 29, 2016.
10. Jellinger PS, Smith DA, Mehta AE, et al.; AACE Task Force for Management of Dyslipidemia and Prevention of Atherosclerosis. American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and Prevention of Atherosclerosis. *AACE Guidelines*. *Endocrine Pract*. 2012;18(Suppl 1):1-78.

Cardiac Risk Assessment Laboratory Tests

11. Kara H, Akinci M, Degirmenci S, et al. High-sensitivity C-reactive protein, lipoprotein-related phospholipase A2, and acute ischemic stroke. *Neuropsychiatr Dis Treat*. 2014 Aug 6;10:1451-7.
12. Katan M, Moon YP, Paik MC, et al. Lipoprotein-associated phospholipase A2 is associated with atherosclerotic stroke risk: the Northern Manhattan Study. *PLoS One*. 2014 Jan 9;9(1):e83393.
13. Kim J, McEvoy JW, Nassir K, et al. Cardiovascular Prospective. Critical Review of High-Sensitivity C-Reactive Protein and Coronary Artery Calcium for the Guidance of Statin Allocation. Head-to-Head Comparison of the JUPITER and St. Francis Heart Trials. American Heart Association. September 16, 2015. Available at: <http://circoutcomes.ahajournals.org/content/7/2/315.full.pdf+html>
14. LeFevre ML. Screening for Asymptomatic Carotid Artery Stenosis: U.S. Preventive Services Task Force (USPSTF) Recommendation Statement Screening for Asymptomatic Carotid Artery Stenosis. *Clinical Guidelines | 2* September 2014. *Ann Intern Med*. 2014;161(5):356-362. doi:10.7326/M14-1333. Available at: <http://annals.org/article.aspx?articleid=1886690>
15. National Institute for Health and Care Excellence (NICE). Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline [CG181] Published date: July 2014 Last updated: September 2016. Available at: <https://www.nice.org.uk/guidance/cg181>
16. National Institute of Health (NIH). National Heart, Lung and Blood Institute. Estimate of 10-Year Risk for Coronary Heart Disease Framingham Point Scores. Available at: <http://www.nhlbi.nih.gov/health-pro/guidelines/current/cholesterol-guidelines/quick-desk-reference-html/10-year-risk-framingham-table>
17. O'Donoghue ML, Morrow DA, Tsimikas S, et al. Lipoprotein(a) for risk assessment in patients with established coronary artery disease. *J Am Coll Cardiol*. 2014;63(6):520-527.
18. Shrivastavaa AK, Singhb HV, Raizadac A, et al. C-reactive protein, inflammation and coronary heart disease. *The Egyptian Heart Journal*. Volume 67, Issue 2, June 2015, Pages 89–97
19. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults. *J Am Coll Cardiol*. 2014; 63(25).
20. Wallentin L, Held C, Armstrong PW, et. al. Lipoprotein associated phospholipase A2 activity is a marker of risk but not a useful target for treatment in patients with stable coronary heart disease. *J Am Heart Assoc* 2016 Jun 21;5(6).pii:e003407. PMID 27329448
21. Arnett D, Blumenthal R, Albert M, et. al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease. *Circulation* 2019;140 e596-e646. PMID 30879355

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in

Cardiac Risk Assessment Laboratory Tests

developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and

Cardiac Risk Assessment Laboratory Tests

LCDs should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.