

Medical Coverage Policy | Measurement of Lipoprotein-Associated Phospholipase A2 in the Assessment of Cardiovascular Risk



EFFECTIVE DATE: 07|01|2024

POLICY LAST REVIEWED: 02|21|2024

OVERVIEW

Lipoprotein-associated phospholipase A2 (Lp-PLA2), also known as platelet-activating factor acetylhydrolase is an enzyme that hydrolyzes phospholipids and is primarily associated with low-density lipoproteins (LDLs). Accumulating evidence has suggested that Lp-PLA2 is a biomarker of coronary artery disease (CAD) and may have a proinflammatory role in the progression of atherosclerosis.

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

Medicare Advantage Plans

Measurement of lipoprotein-associated phospholipase A2 (Lp-PLA2) is not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

Commercial Products

Measurement of lipoprotein-associated phospholipase A2 (Lp-PLA2) is considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. §27-19-81 described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

BACKGROUND

Low-density lipoproteins (LDL) have been identified as the major atherogenic lipoproteins and have long been identified by the National Cholesterol Education Project (NCEP) as the primary target of cholesterol lowering therapy. LDL particles consist of a surface coat composed of phospholipids, free cholesterol, and apolipoproteins surrounding an inner lipid core composed of cholesterol ester and triglycerides. Traditional lipid risk factors such as low-density lipoprotein-cholesterol (LDL-C), while predictive on a population basis, are weaker markers of risk on an individual basis. Only a minority of subjects with elevated LDL and cholesterol levels will develop clinical disease, and up to 50% of cases of coronary artery disease (CAD) occur in subjects with 'normal' levels of total and LDL cholesterol.

Although treatment for elevated coronary disease risk with statins targets cholesterol levels, selection for treatment involves estimation of future CAD risk using well-validated prediction models that use additional variables.

Lipoprotein-associated phospholipase A2 (Lp-PLA2), also known as platelet-activating factor acetylhydrolase, is an enzyme that hydrolyzes phospholipids and is primarily associated with LDLs. Accumulating evidence has suggested that Lp-PLA2 is a biomarker of CAD and may have a proinflammatory role in the progression of atherosclerosis. Recognition that atherosclerosis represents, in part, an inflammatory process has created considerable interest in measurement of proinflammatory factors as part of cardiovascular disease risk assessment.

Interest in Lp-PLA2 as a possibly causal risk factor for CAD has generated development and testing of Lp-PLA2 inhibitors as a new class of drugs to reduce risk of CAD. However, clinical trials of Lp-PLA2 inhibitors have not shown significant reductions in CAD end points. Furthermore, assessment of Lp-PLA2 levels has not been used in the selection or management of subjects in the clinical trials.

For individuals who have a risk of cardiovascular disease who receive Lp-PLA2 testing, the evidence includes studies of the association between Lp-PLA2 and various coronary artery disease outcomes. Relevant outcomes are overall survival, disease-specific survival, and test validity. The studies have demonstrated that Lp-PLA2 levels are an independent predictor of cardiovascular disease. Although Lp-PLA2 levels are associated with cardiovascular disease risk, changes in patient management that would occur as a result of obtaining Lp-PLA2 levels in practice are not well-defined. To demonstrate clinical utility, clinicians must have the tools to incorporate Lp-PLA2 test results into existing risk prediction models that improve classification into risk categories alter treatment decisions and lead to improved health outcomes. Direct evidence for such improved health outcomes with Lp-PLA2 testing in clinical practice is lacking. The evidence is insufficient to determine the effects of the technology on health outcomes. Therefore, this service is not covered for Medicare Advantage Plans and not medically necessary for Commercial products.

CODING

The following code(s) is not covered for Medicare Advantage Plans and not medically necessary for Commercial Products:

83698 Lipoprotein-associated phospholipase A₂ (Lp-PLA₂)

RELATED POLICIES

Biomarker Testing Mandate
Genetic Testing Services

PUBLISHED

Provider Update, April 2024
Provider Update, March 2023, November 2023
Provider Update, April 2022
Provider Update, March 2021
Provider Update, March 2020

REFERENCES

1. White HD, Held C, Stewart R, et al. Darapladib for preventing ischemic events in stable coronary heart disease. *N Engl J Med*. May 01 2014; 370(18): 1702-11. PMID 24678955
2. O'Donoghue ML, Braunwald E, White HD, et al. Effect of darapladib on major coronary events after an acute coronary syndrome: the SOLID-TIMI 52 randomized clinical trial. *JAMA*. Sep 10 2014; 312(10): 1006-15. PMID 25173516

3. Nicholls SJ, Kastelein JJ, Schwartz GG, et al. Varespladib and cardiovascular events in patients with an acute coronary syndrome: the VISTA-16 randomized clinical trial. *JAMA*. Jan 15 2014; 311(3): 252-62. PMID 24247616
4. National Institutes of Health, National Heart Lung and Blood Institute. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (NIH Publication No. 01-3670). 2001; <http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf> Accessed November 17, 2023.
5. Di Angelantonio E, Gao P, Pennells L, et al. Lipid-related markers and cardiovascular disease prediction. *JAMA*. Jun 20 2012;307(23): 2499-506. PMID 22797450
6. Thompson A, Gao P, Orfei L, et al. Lipoprotein-associated phospholipase A(2) and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. *Lancet*. May 01 2010; 375(9725): 1536-44. PMID 20435228
7. Garza CA, Montori VM, McConnell JP, et al. Association between lipoprotein-associated phospholipase A2 and cardiovascular disease: a systematic review. *Mayo Clin Proc*. Feb 2007; 82(2): 159-65. PMID 17290721
8. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. Sep 10 2019; 140(11): e596-e646. PMID 30879355
9. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. Dec 14 2010; 56(25): e50-103. PMID 21144964
10. Jellinger PS, Handelsman Y, Rosenblit PD, et al. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF CARDIOVASCULAR DISEASE. *Endocr Pract*. Apr 2017; 23(Suppl 2): 1-87. PMID 28437620
11. Jellinger PS, Smith DA, Mehta AE, et al. American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and Prevention of Atherosclerosis. *Endocr Pract*. Mar-Apr 2012; 18 Suppl 1: 1-78. PMID 22522068

CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS

This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member's subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.

