



MASSACHUSETTS

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Medical Policy

Measurement of Lipoprotein-Associated Phospholipase A2 in the Assessment of Cardiovascular Risk

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Policy Number: 558

BCBSA Reference Number: 2.04.32 (For Plan internal use only)

Related Policies

Novel Lipid Risk Factors in Risk Assessment and Management of Cardiovascular Disease #[283](#)

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Measurement of lipoprotein-associated phospholipase A₂ is considered [INVESTIGATIONAL](#).

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is not a covered service.
Commercial PPO and Indemnity	This is not a covered service.
Medicare HMO BlueSM	This is not a covered service.
Medicare PPO BlueSM	This is not a covered service.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

CPT codes:	Code Description
83698	Lipoprotein-associated phospholipase A2 (Lp-PLA2)

Description

Low-Density Lipoproteins

Low-density lipoproteins (LDLs) have been identified as major atherogenic lipoproteins and have long been identified by the National Cholesterol Education Project 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, 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 low-density lipoprotein cholesterol.

Treatment

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 the measurement of pro-inflammatory factors as part of cardiovascular disease risk assessment.

Interest in Lp-PLA₂ as a possible causal risk factor for CAD has generated the development and testing of Lp-PLA₂ inhibitors as a new class of drugs to reduce the risk of CAD. However, clinical trials of Lp-PLA₂ inhibitors have not shown significant reductions in CAD endpoints.^{1,2,3} Furthermore, assessment of Lp-PLA₂ levels has not been used in the selection or management of subjects in the clinical trials.

Summary

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. Accumulating evidence has suggested that Lp-PLA₂ is a biomarker of coronary artery disease and may have a proinflammatory role in the progression of atherosclerosis.

Summary of Evidence

For individuals who have a risk of CVD who receive Lp-PLA₂ testing, the evidence includes studies of the association between Lp-PLA₂ and various CAD 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 CVD. Although Lp-PLA₂ levels are associated with CVD 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 that the technology results in an improvement in the net health outcomes.

Policy History

Date	Action
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2/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
2/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
2/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2018	Annual policy review. New references added.
1/2017	Annual policy review. New references added.
8/2015	Annual policy review. New references added.
9/2014	Annual policy review. New references added.
8/2013	Annual policy review. New references added.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
4/2011	Reviewed - Medical Policy Group – Cardiology and Pulmonology. No changes to policy statements.
10/20/2010	New policy, effective 10/20/2010 describing ongoing non-coverage.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

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 22, 2021
5. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Special Report: C-Reactive Protein as a Cardiac Risk Marker. TEC Assessment. 2002;17:Tab 23.
6. 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
7. 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
8. 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
9. 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

10. 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
11. 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
12. 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
13. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention Rehabilitation (EACPR). *Eur Heart J*. Aug 01 2016; 37(29): 2315-2381. PMID 27222591