

Corporate Medical Policy

Lipoprotein-associated Phospholipase A2

File Name: lipoprotein_associated_phospholipase_a2
Origination: 1/2007
Last CAP Review: 10/2011
Next CAP Review: 10/2012
Last Review: 10/2011

Description of Procedure or Service

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

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 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 occur in subjects with “normal” levels of total and LDL cholesterol. Thus there is considerable potential to improve the accuracy of current cardiovascular risk prediction models.

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*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC does not cover measurement of lipoprotein-associated phospholipase A2. It is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

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When Lipoprotein-associated Phospholipase A2 is covered

Not Applicable

When Lipoprotein-associated Phospholipase A2 is not covered

Measurement of lipoprotein-associated phospholipase A2 (Lp-PLA2) in the assessment of cardiovascular risk is considered investigational.

Policy Guidelines

A review of the literature regarding Lp-PLA2 was completed through September 2010. None of the reviewed studies provide evidence that would lead to a change in the current policy statement. The risk prediction studies corroborate previous research demonstrating that Lp-PLA2 is an independent predictor of cardiovascular disease, but do not demonstrate that health outcomes are improved as a result of measuring Lp-PLA2.

The key outcome of cardiac risk assessment is an improvement in health outcomes. Improved risk prediction does not by itself result in improved health outcomes. To improve outcomes, clinicians must have the tools to translate this information into clinical practice. To do this requires guidelines that incorporate emerging risk factors into existing risk prediction models and that have been demonstrated to classify patients into risk categories with greater accuracy. Predictive models also need to be accompanied by treatment guidelines that target intervention toward patients who will get the most benefit. At present, measurements of Lp-PLA2 are not a component of the guidelines developed by the National Cholesterol Education Program Adult Treatment Panel III.

Clinical trials of Lp-PLA2 inhibitors are a new line of research with therapeutic potential. However, the available trials are preliminary, reporting only on physiologic outcomes such as reduction in hs-CRP, and using a pharmacologic agent that is not yet approved for use in the U.S. Further clinical trials that utilize clinical outcomes as the primary endpoint(s) are currently in progress. At least three phase III clinical trials that utilize clinical outcomes as the primary endpoint(s) are currently in progress, and results from these may be available starting in 2012.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 83698

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.32, 4/25/06

Packard CJ, O'Reilly DS, Caslake MJ, McMahon AD, Ford I, Cooney J, et al. Lipoprotein-

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associated phospholipase A2 as an independent predictor of coronary heart disease. *N Engl J Med.* 2000 Oct 19;343(16):1148-55

U.S. Food and Drug Administration. 510(k) Summary diaDexus PLAC® Test. Retrieved 12/20/06 from www.fda.gov/cdrh/pdf6/K062234.pdf

BCBSA TEC Assessment [Electronic Version]. Special Report: High-Sensitivity C-Reactive Protein Measurement for Coronary Heart Disease Risk Stratification. May 2003.

U.S. Department of Health and Human Services, National Institutes of Health (NIH), National Heart, Lung and Blood Institute (NHLBI). 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). Final Report. NIH Publication No. 02-5215. September 2002. Retrieved 1/4/07 from http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm

Institute for Clinical Systems Improvement (ICSI). Biochemical markers of cardiovascular disease risk. Technology Assessment Report No. 66. January 2003. Retrieved 1/4/07 from http://www.icsi.org/display_file.asp?FileId=716&title=TA%20Biochemical%20Markers%20of%20Cardiovascular%20Disease%20Risk

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.32, 12/12/06

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.32, 10/07/08

The Lp-PLA2 Studies Collaboration. Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. *Lancet* 2010; 375(9725):1536-44.

Suckling KE. Phospholipase A2 inhibitors in the treatment of atherosclerosis: a new approach moves forward in the clinic. *Expert Opin Investig Drugs* 2009; 18(10):1425-30.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.32, 6/10/10

Specialty Matched Consultant Advisory Panel review 10/2010

Hatoum IJ, Cook NR, Nelson JJ et al. Lipoprotein-associated phospholipase A2 activity improves risk discrimination of incident coronary heart disease among women. *Am Heart J* 2011; 161(3):516-22.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.32, 6/9/11

The Lp-PLA2 Studies Collaboration. Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. *Lancet* 2010; 375(9725):1536-44.

National Institutes of Health (NIH). The Stabilization Of pLaques usIng Darapladib-Thrombolysis In Myocardial Infarction 52 Trial (SOLID-TIMI 52). Clinical Trial # NCT01000727. Retrieved on September 16, 2011 from <http://clinicaltrials.gov/ct2/show/NCT01000727?term=SOLID-TIMI+52&rank=1>

Specialty Matched Consultant Advisory Panel review 10/2011

Policy Implementation/Update Information

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- 1/29/07 New policy issued. Measurement of lipoprotein-associated phospholipase A2 (Lp-PLA2) in the assessment of cardiovascular risk is considered investigational. (adn)
- 11/19/07 Additional information added to Policy Guidelines section to support continued investigational status. Specialty Matched Consultant Advisory Panel review meeting 10/29/07. Policy accepted as written. (adn)
- 12/7/09 Specialty Matched Consultant Advisory Panel review meeting 10/30/09. No change to policy statement. (adn)
- 6/22/10 Policy Number(s) removed (amw)
- 11/23/10 Specialty Matched Consultant Advisory Panel review 10/2010. Description section and Policy Guidelines section updated. References updated. (mco)
- 8/30/11 References updated. Policy Guidelines updated with information regarding on-going clinical trials. (mco)
- 11/8/11 References updated. Specialty Matched Consultant Advisory Panel review 10/2011. No changes to Policy Statements. (mco)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.