

## FEP 2.04.32 Measurement of Lipoprotein-Associated Phospholipase A2 in the Assessment of Cardiovascular Risk

**Effective Date:** April 15, 2018

**Related Policies:**

2.04.65 Novel Lipid Risk Factors in Risk Assessment and Management of Cardiovascular Disease  
2.04.70 Genetic Testing for Lipoprotein(a) Variants as a Decision Aid for Aspirin Treatment

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

### Description

Lipoprotein-associated phospholipase A<sub>2</sub> (Lp-PLA<sub>2</sub>), 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-PLA<sub>2</sub> is a biomarker of coronary artery disease and may have a proinflammatory role in the progression of atherosclerosis.

### FDA REGULATORY STATUS

In December 2014, the PLAC® Test (diaDexus, San Francisco, CA), a quantitative enzyme assay, was cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process for Lp-PLA<sub>2</sub> activity. It was considered substantially equivalent to a previous version of the PLAC® Test (diaDexus), which was cleared for marketing by the Food and Drug Administration in July 2003.

### POLICY STATEMENT

Measurement of lipoprotein-associated phospholipase A<sub>2</sub> is considered **investigational**.

### POLICY GUIDELINES

Measurement of lipoprotein (a) enzyme is a distinct laboratory test. Measurement of lipoprotein (a) enzyme is addressed in evidence review 2.04.65, and genetic testing for lipoprotein (a) variants is addressed in evidence review 2.04.70.

### BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

### RATIONALE

#### Summary of Evidence

For individuals who have a risk of cardiovascular disease who receive Lp-PLA<sub>2</sub> testing, the evidence includes studies of technical reliability and studies of the association between Lp-PLA<sub>2</sub> and various coronary artery disease outcomes. Relevant outcomes are overall survival, disease-specific survival, and test validity. The studies have demonstrated that Lp-PLA<sub>2</sub> levels are an independent

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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.

### SUPPLEMENTAL INFORMATION

#### Practice Guidelines and Position Statements

##### American College of Cardiology and American Heart Association

The American College of Cardiology and American Heart Association published joint guidelines on the assessment of cardiovascular risk in asymptomatic patients in 2013.<sup>39</sup> Lipoprotein-associated phospholipase A<sub>2</sub> (Lp-PLA2) testing was not mentioned in these guidelines, which was a change from 2010 guidelines.<sup>40</sup> In their prior guideline, Lp-PLA2 was given an IIb recommendation for assessing cardiovascular risk in intermediate-risk asymptomatic adults.

##### American Association of Clinical Endocrinologists

The American Association of Clinical Endocrinologists published guidelines on the management of dyslipidemia and prevention of atherosclerosis in 2012.<sup>41</sup> These guidelines made the following recommendations for Lp-PLA2 testing (see Table 1).

**Table 1. Guidelines on Dyslipidemia and Atherosclerosis**

Recommendation	GOE	LOE
Assess markers of inflammation in patients where further stratification of risk is necessary. Highly sensitive CRP (hsCRP) and Lp-PLA2 provide useful information in these instances and appear to be synergistic in predicting risk of CVD and stroke	B	1
Measure Lp-PLA2, which in some studies has demonstrated more specificity than hsCRP, when it is necessary to further stratify a patient's CVD risk, especially in the presence of systemic highly sensitive CRP elevations	B	2

CRP: C-reactive protein; CVD: cardiovascular disease; GOE: grade of evidence; LOE: level of evidence; Lp-PLA2: lipoprotein-associated phospholipase A<sub>2</sub>.

A 2017 update to guidelines published jointly by the American Association of Clinical Endocrinologists and American College of Endocrinology recommended the measurement of Lp-PLA2 as an additional indication of cardiovascular risk.<sup>42</sup> Citing several studies in which Lp-PLA2 was comparable with high-sensitivity C-reactive protein as a risk predictor, the guidelines accordingly recommended the use of Lp-PLA2 data in situations requiring a more specific evaluation of risk of atherosclerotic cardiovascular disease that is provided by high-sensitivity C-reactive protein.

##### European Society of Cardiology et al

In 2012, the European Society of Cardiology and other cardiovascular disease societies issued clinical practice guidelines on cardiovascular disease prevention.<sup>43</sup> These guidelines included the following statement about Lp-PLA2 testing:

- LpPLA2 may be measured as part of a refined risk assessment in patients at high risk of a recurrent acute atherothrombotic event (*Class IIb recommendation; Level of Evidence B; weak evidence*).

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### U.S. Preventive Services Task Force Recommendations

No U.S. Preventive Services Task Force recommendations on the use of Lp-PLA2 in the assessment of cardiovascular risk have been identified.

### Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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### POLICY HISTORY

Date	Action	Description
December 2011	New Policy	
June 2012	Update Policy	
September 2013	Update Policy	Policy statement changed to not medically necessary. Updated literature search. Reference 19 added. Policy updated with literature search; references added. No change to policy statement.
September 2014	Update Policy	Policy updated with literature search, adding references 3, 20-22, 39 and 42. No change to policy statement.
September 2015	Update Policy	Policy updated with literature review through May 11, 2015. References 34, 37, and 39 added. Policy statement unchanged.
March 2017	Update Policy	Policy updated with literature review; reference 38 added. Policy statement changed to investigational.
March 2018	Update Policy	Policy updated with literature review through October 16, 2017; reference 42 added. Policy statement unchanged

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