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Developed By: Medical Criteria Committee	

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Approved:

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Description:

The traditional risk factors for cardiovascular disease include smoking, hypertension, diabetes, obesity, age, family history, lipid abnormalities and sedentary lifestyle. Nearly half of the patients that present with a myocardial infarction do not have these classic risk factors. This finding has directed research to look for other risk factors that may be responsible for coronary artery disease and to develop screening tests to predict future coronary events in healthy individuals. Several nontraditional markers of cardiovascular risk have been developed to improve identification of patients at high risk. These include the following laboratory tests:

High Sensitivity C-reactive protein (hs-CRP): (CPT 86141) It is thought that certain markers of inflammation may indicate the development of atherosclerosis. High sensitivity C-reactive protein is a systemic marker of inflammation that has been used as a screening test for assessing cardiovascular disease risk.

Homocysteine: (CPT 83090) is an amino acid normally found in the body. Studies suggest that high blood levels of homocysteine may increase an individual's chance of developing heart disease, stroke and damage to arteries.

Apolipoprotein A-I, LDL gradient gel electrophoresis, and Lipoprotein (a) immunoassay: (CPT 82172, 83695) these tests are performed to help determine coronary heart disease risk and to guide drug and diet therapy in patients with established coronary artery disease.

Apolipoprotein B: is thought to be a useful risk assessment tool in patients with normal LDL who have a high family risk for premature coronary artery disease. However, apo B assays have not been fully standardized and there is no consensus on predictive or treatment value. Apolipoprotein E polymorphisms have functional effects on lipoprotein metabolism and have been studied in disorders associated with elevated cholesterol levels and lipid derangements. Research investigators have found that the apo E genotype yields poor predictive values when screening for clinically defined atherosclerosis.

LDL subspecies: Larger and smaller low-density lipoprotein (LDL) particle size may be associated with coronary heart disease. In addition, nearly half of patients with coronary atherosclerotic disease have dense LDL particles. When present, dense LDL greatly increases the risk of coronary disease.

HDL subspecies: High-density lipoprotein (HDL) is known as the "good cholesterol", however, not all HDL is beneficial. HDL subfractions (lipoprotein AI (LpAI) and lipoprotein AI/AII (LpAI/AII) and/or HDL3 and HDL2) have also been used for risk prediction. However, studies have not shown superiority of HDL subspecies over HDL cholesterol in CHD risk assessments.

Angiotensin gene (AGT) or CardiaRisk: This test analyzes angiotensin gene polymorphisms which have been associated with cardiovascular disease risk and some forms of hypertension. Certain AGT polymorphisms have been associated with responsiveness of blood pressure to ACE inhibitor therapy and sodium reduction. Therefore, analysis of the AGT gene may be beneficial in helping to predict how patients will respond to certain antihypertensive interventions. CardiaRisk is a lab test done at Myriad Genetics Laboratories that analyzes the angiotensinogen gene.

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Criteria:

- I. ODS will cover hs-CRP as a medical diagnostic only. hs-CRP is considered investigational and will not be covered when performed as a routine screening test.

- II. Other laboratory tests for assessing coronary heart disease are considered investigational for screening, diagnosing, or managing coronary heart disease. However, ODS will allow limited coverage of specific tests under the following circumstances:
 - A. Lipoprotein (a) and hs-CRP will be covered for young individuals who have unexplained coronary artery disease and lack traditional risk factors.
 - B. Lipoprotein (a) will be covered for members with the diagnosis of complex lipid disorder with familial hyperlipidemia, such as Familial Lp (a) hyperlipidemia.
 - C. Homocysteine will be covered for members undergoing workup or management of suspected homocystinurias or for a hypercoagulable workup (i.e. members with unexplained deep vein thrombosis or recurrent thrombosis).
 - D. Apolipoprotein B will be covered for members undergoing management of lipoprotein abnormalities **and** who have one of the following:
 1. Diabetes; or
 2. Coronary heart disease; or
 3. Member is a smoker; or
 4. Member has a family history of premature coronary heart disease

Information to be Submitted with Pre-Authorization Request:

Documentation from the ordering physician supporting one of the above listed indications.

When performed as a routine screening, these tests are considered investigational and will not be covered. Prevailing medical literature does not support the use of these tests for screening of coronary heart disease.

References:

- Guthrie RM. Counseling patients about lipid management. Part 1. What are the goals of therapy? Medical World Communications. May 2003.
- Grundy, et al. AHA/ACC Scientific statement: assessment of cardiovascular risk by use of multiple-risk-factor assessment equations. J. American College of Cardiology. 1999; 34:1348-59.
- www.berkeleyheartlab.com
- www.preventivecardiology.com/global_risk.htm
- Does C-reactive protein predict cardiovascular risk better than LDL? Hayes Alert; Dec. 2002; 5(12).
- Nontraditional markers of cardiovascular risk. Diabetes Forum. 2002; 1(2).
- Risk Factors for Atherosclerotic Disease, A Textbook of Cardiovascular Medicine, 6th ed., 2001, Ch. 31.
- Pearson TA, et al. Markers of inflammation and cardiovascular disease. American Heart Association 2003.
- Durga J, van Tits L, Schouten E, et al. Effect of lowering of homocysteine levels on inflammatory markers: A randomized controlled trial. Arch Intern Med. June 27, 2005; 165:1388-1394.
- C-reactive protein as a predictor for atherosclerotic progression and recurrent cardiac events. Hayes Alert. January 2005; 8(1):3-4.
- Danesh J, Wheeler J, Hirschfield G, et al. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. The New England Journal of Medicine. April 2004; 350(14):1387-1397.
- Pai J, Pischon T, Ma J, et al. Inflammatory markers and the risk of coronary heart disease in men and women. The New England Journal of Medicine. December 2004; 351(25):2599-2610.
- Ridker P, Hennekens C, Buring J. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. The New England Journal of Medicine. March 2000; 342:836-843.

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- Ridker P, Block P. CRP in 2005. Expert opinions. Cardiosource American College of Cardiology. July 2005. www.cardiosource.com
- Physician Advisors