MEDICAL POLICY STATEMENT

Original Effective Date	Next Annual Review Date	Last Review / Revision Date
11/17/2015	11/17/2016	11/17/2015

Policy Name	Policy Number
Lipid Testing in Assessing Cardiovascular (CV) Risk	MM-0012

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For Medicare plans please reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

A. SUBJECT

Lipid Testing in Assessing Cardiovascular (CV) Risk

B. BACKGROUND

Appropriate screening for identifying individuals at risk of developing cardiovascular diseases (CVD) including coronary artery disease, stroke, and hypertension is important because vascular disorders are a preventable cause of mortality and morbidity. The life-time risk of developing CVD is high (estimated to be 66% for men and >50% for women). The ideal screening tool for assessment of CVD risk should be accurate and cost-effective. There have been rapid developments in the understanding of appropriate cardiac screening tests. For example the American College of Preventive Medicine (ACPM) in a publication dated 2011 recommends the use of a CHD risk assessment tool such as the Framingham Risk Score, while the most recent guidelines from the ACC/AHA (2013) recommend a more robust risk calculator. In line with the ACC/AHA guidelines CareSource considers lipid testing as a medically necessary component for certain groups of patients to assess their risk of development of CVD.

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality in the United States. Vascular disease is the major contributor to CVD events. Early identification, prior to symptoms, assist in preventing irreversible cardiovascular damage. Cholesterol is a fat-like substance (lipid) present in cell membranes found in blood which is a primary contributor to CVD. In addition, small and large arterial compliance is affected by arterial stiffness, which also impacts CVD.

Lipid testing is utilized to indicate the chances of having cardiovascular disease (CVD) and/or of having a coronary event. The most common blood tests (often referred to as a *basic* or *standard lipid panel*) to determine cardiac risk are **high-density lipoprotein (HDL)**, **low-density lipoprotein (LDL)**, **total cholesterol,** and **triglycerides**. Additional lab tests that

have been studied for cardiovascular risk which may be unrelated to this policy include, but may not be limited to, the following:

- **Apolipoprotein testing** - An apolipoprotein is any of various proteins that combines with a lipid to form a lipoprotein, such as HDL or LDL. Apolipoproteins are important in the transport of cholesterol in the body and the regulation of the level of cholesterol in cells and blood. They are suggested as possible indicators of cardiovascular risk. The types of apolipoproteins are:
  - **Apolipoprotein A-1 (apo A-1)** - The major protein component of HDL and a relatively abundant plasma protein. Apo-A1 is instrumental in promoting the transfer of cholesterol into the liver where it is metabolized and then excreted from the body via the intestine.
  - **Apolipoprotein B (apo B)** - The primary apolipoprotein of LDL, which is responsible for carrying cholesterol to tissues.
  - **Apolipoprotein E (apo E)** - A type of lipoprotein that is a major component of very low density lipoproteins (VLDL). Apo E is essential for the normal catabolism (breaking down) of triglyceride-rich lipoprotein constituents (components). A major function of VLDL is to remove excess cholesterol from the blood and carry it to the liver for processing.
- **Comprehensive lipid panel testing (e.g., VAP)** - May include various tests such as apolipoproteins, HDL, homocysteine, LDL, lipoprotein remnants, lipoprotein subfractions, Lp(a), Lp-PLA2, and triglycerides.
- **Fibrinogen testing** - Fibrinogen is a protein in the blood that helps blood clot. Too much fibrinogen may promote excessive clumping of platelets. This can cause clots to form in an artery, which may lead to heart attack or stroke. Suggested as a possible indicator of inflammation that accompanies atherosclerosis.
- **Galectin-3 testing** - A protein that is associated with the development and progression of heart failure, including progressive fibrosis (stiffening) of the heart muscle. Testing purportedly assists in assessing the prognosis of chronic heart failure. Studies related to galectin-3 levels report increases were associated with worse outcomes and may detect late or irreversible disease not responding to therapy.
- **Homocysteine testing** - Homocysteine is an amino acid used to make protein and to build and maintain tissue. Excess levels in the blood are purported to increase the risk of stroke, certain types of heart disease, or peripheral artery disease (PAD).
- **LDL-P (LDL particle number)** measures the actual number of LDL particles (particle concentration, nmol/L).
- **Lipoprotein-associated phospholipase A2 (Lp-PLA2** or **PLAC) testing** - An enzyme immunoassay for the quantitative determination of Lp-PLA2 in plasma; used in conjunction with clinical evaluation and patient risk assessment as a suggested aid in predicting risk for coronary heart disease (CHD).
- **Lipoprotein(a) testing (Lp[a])** - An LDL cholesterol particle that is attached to a special protein called apo A. Elevated levels in the blood are purportedly linked to a greater likelihood of atherosclerosis and heart attacks.
- **Lipoprotein remnants testing** - Triglyceride-rich lipoproteins that include intermediate density lipoproteins (IDL) and VLDL. It is proposed that lipoprotein remnants penetrate arterial walls more easily than larger lipoproteins and may be independent risk factors for CVD.
- **Lipoprotein subfraction testing** - Testing that separates two of the commonly measured lipoprotein fractions, HDL and LDL, into subclasses based on their size, density, and/or electrical charge:
- **HDL subclass testing** - Suggested to provide information regarding CVD risk when utilized with standard lipoprotein tests, such as total cholesterol, HDL, and LDL testing.

- **LDL subclass testing** - Suggested as part of an overall risk assessment for CVD, this test measures the cholesterol content of lipoprotein particles in the blood and determines the LDL particle size and/or density pattern.
- **Long-chain omega-3 fatty acids testing** - A family of unsaturated fatty acids that have in common a carbon-carbon double bond in the third bond from the methyl end of the fatty acid. Omega-3 fatty acids cannot be manufactured by the body and are obtained from foods such as fish (e.g., salmon, halibut), certain plants, and nut oils. Suggested as a cardiac risk factor for sudden cardiac death.
- **Skin cholesterol test (PREVU) testing** - An in vitro diagnostic test and the only noninvasive method to assess skin cholesterol. Suggested to assess risk of CAD in patients with a history of heart attack or with clinical symptoms or signs of CAD.

C. DEFINITIONS

- **Cholesterol** - White, crystalline substance found in animal tissues and various foods that is normally synthesized by the liver and is important as a constituent of cell membrane and a precursor to steroid hormones; its level in the bloodstream can influence the pathogenesis of certain conditions, such as the development of atherosclerotic plaque and coronary artery disease.
- **Coronary Heart Disease (CHD) -** Any heart disorder caused by disease of the coronary arteries.
- **High Density Lipoprotein (HDL)** - A lipoprotein that transports cholesterol in the blood; composed of a high proportion of protein and relatively little cholesterol. High levels are thought to be associated with decreased risk of CHD and atherosclerosis.
- **High-sensitivity C-reactive protein (hs-CRP)**- A protein produced in the liver that is a marker of inflammation.
- **Immunoassay** - Any laboratory method for detecting a substance by using an antibody reactive with it.
- **Lipid** - Oily organic compound insoluble in water but soluble in organic solvents; essential structural component of living cells (along with proteins and carbohydrates).
- **Low Density Lipoprotein (LDL)** - A lipoprotein that transports cholesterol in the blood; composed of a moderate amount of protein and a large amount of cholesterol. High levels are thought to be associated with increased risk of CHD and atherosclerosis.
- **Peripheral Arterial Disease (PAD)** - A narrowing of the vessels that carry blood to the legs, arms, abdomen or kidneys; also known as peripheral vascular disease (PVD).
- **Plaque** - Deposit of fatty material on the inner lining of an arterial wall; characteristic of atherosclerosis.
- **Triglyceride** – Naturally occurring ester (compound) of three fatty acids and glycerol that is the chief constituent of fats and oils.
- **Unsaturated** - Capable of taking up, or of uniting with, certain other elements or compounds, without the elimination of any side.

D. POLICY

The new ACC/AHA guidelines cited above identify four separate groups of patients who may benefit from the use of a statin medication to reduce cardiovascular risk: (1) Individuals with clinical atherosclerotic cardiovascular disease (ASCVD), (2) individuals with primary elevation of low-density lipoprotein cholesterol (LDL-C) higher than 190 mg/dL, (3) Individuals aged 40-75 years with diabetes with an LDL-C between 70 and 189 mg/dL, and (4) individuals without clinical ASCVD or diabetes aged 40-75 years with an LDL-C from 70-189 mg/dL and an estimated 10-year atherosclerotic cardiovascular risk (as identified by a risk calculator) of 7.5% or greater. The guidelines also recommend that in a non-fasting individual, a non-HDL-C of more than 220 mg/dL may indicate genetic hypercholesterolemia

that requires further evaluation.

Also the ACC/AHA panel recommends that treatment decisions in selected individuals who are not included in the four categories of statin benefit can also be informed by other factors, including biochemical and non-invasive testing such as coronary artery calcium score. The panel did not endorse the use of apolipoprotein B, LDL particle measurements, or other lipid measurements, however it did suggest the measurement of high-sensitivity C-reactive protein (hs-CRP) in patients with an intermediate risk of development of CVD, with a cutoff of >2 mg/L denoting greater risk. These patients may also benefit from statin therapy.

Triglyceride testing is required for the calculation of the LDL-C component of the lipid profile.

CareSource members may be eligible under the Plan for **standard lipid panel testing, which includes HDL, LDL, total cholesterol,** and **triglycerides** to determine cardiovascular risk.

Note: The criteria for **CVD lipid testing** are not consistent with the Medicare National Coverage Policy, and therefore may not be applicable to Medicare members. Refer to the CMS website at http://www.cms.hhs.gov for additional information.

CareSource members may **NOT** be eligible under the Plan for **CVD lipid testing** listed below or for any other testing or indications other than those listed above. These technologies are considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition.

Note: ***Non-covered*** tests related to this policy include, but may not be limited to, the following:

- Apolipoprotein A-1 (apo A-1)
- Apolipoprotein E (apo E)
- Comprehensive lipid panel (e.g., VAP)
- Fibrinogen
- Galectin-3
- HDL subclass
- Homocysteine
- LDL subclasses (e.g., NMR)
- Lipoprotein(a) (Lp[a])
- Lipoprotein-associated phospholipase A2 (Lp-PLA2 or PLAC
- Lipoprotein remnants - intermediate density lipoproteins (IDL) and small densitylipoproteins)
- Long-chain omega-3 fatty acids
- Skin cholesterol (e.g., PREVU)

For Medicare Plan members, reference the Applicable National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). Compliance with NCDs and LCDs is required where applicable.
NCD: 190.23

CONDITIONS OF COVERAGE

HCPCS
CPT

AUTHORIZATION PERIOD

E. REVIEW/REVISION HISTORY

Date Issued: 11/17/2015
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Date Revised:

F. REFERENCES

1. Lipoprotein-Associated Phospholipase Testing for Coronary Heart Disease Risk Assessment in Healthy or Asymptomatic Adults. (2010, January 1). Retrieved from https://www.hayesinc.com/subscribers/subscriberArticlePDF.pdf?articleId=11917
2. Galectin-3 In Vitro Diagnostic Assay (BG Medicine Inc.) for the Management of Patients with Chronic Heart Failure. (2010, January 1). Retrieved from https://www.hayesinc.com/subscribers/subscriberArticlePDF.pdf?articleId=15848
3. Contois, J., McConnell, J., Sethi, A., Csako, G., Devaraj, S., Hoefner, D., & Warnick, G. (2009, March 1). Apolipoprotein B and Cardiovascular Disease Risk: Position Statement from the AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. Retrieved October 23, 2014, from http://www.clinchem.org/content/55/3/407.long
4. Am J Prev Med. 2011 Mar;40(3):381.e1-10.
5. Journal of the American College of Cardiology, Volume 63, Issue 25, Part B, 1 July 2014, Pages 2889-2934

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.

Independent medical review – 2/2015