LIPID TESTING
Policy Number: CMP-012
Effective Date: January 1, 2018

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INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee’s document (e.g., Certificate of Coverage (COC) or Summary Plan Description (SPD)) may differ greatly. In the event of a conflict, the enrollee's specific benefit document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BACKGROUND

Cardiovascular disease (CVD; e.g., heart and blood vessel disease) includes numerous problems, many of which are related to a process called atherosclerosis. Atherosclerosis is a condition that develops when plaque builds up in the walls of the arteries. Plaque is made up of fat, cholesterol, calcium, and other substances found in the blood. As atherosclerosis progresses some plaques will become unstable and these unstable plaques may experience sudden rupture leading to clot formation and acute interruption in blood flow. Alternatively, some plaques will slowly increase in size without becoming unstable. Some stable plaques may enlarge to the point where they substantially limit blood flow resulting in angina type symptoms.

Heart disease is the leading cause of death in the United States for men and women. Mortality data show that CVD accounted for 33.6% (813,804) of over 2 million deaths in 2007, or 1 of every 2.9 deaths in the United States. Furthermore, more than 2,200 people die of CVD each day, an average of 1 death every 39 seconds.
A wide variety of modifiable and non-modifiable risk factors are associated with increased cardiovascular risk including: age, race, gender, family history of heart disease, elevated LDL, decreased HDL, high blood pressure, diabetes and prediabetes, chronic kidney disease, overweight and obesity, smoking, substance abuse, lack of physical activity, unhealthy diet, and stress. The risk of heart disease increases with age and men have a higher risk of having heart disease than pre-menopausal women. However, after menopause, the risk for women is closer to the risk for men. The simultaneous presence of multiple risk factors, as well as increasing exposure to risk factors over time, further increase the magnitude of cardiovascular risk. Additionally, several racial groups have a higher risk for heart disease including African Americans, Mexican Americans, American Indians, Hawaiians, and some Asian Americans.

**Relationship of Lipids and Cardiovascular Disease**

Lipoprotein particles that carry cholesterol and triglycerides are the direct mediators of the atherosclerotic process. Low-density lipoprotein (LDL) particles, and to a lesser degree intermediate-density lipoprotein (IDL) and remnant particles, promote and accelerate atherosclerosis by entering the artery wall, becoming oxidized, and subsequently being ingested by macrophages, creating cholesterol-rich foam cells that develop into atherosclerotic plaque. High-density lipoprotein (HDL) particles entering the artery wall prevent or reverse this process by, among other actions, inhibiting the oxidation of LDL particles and removing cholesterol from the foam cells for delivery back to the liver via a process called reverse cholesterol transport. Various triglyceride (TG) rich lipoproteins are also associated with increased CVD risk, although is unclear whether these particles are directly related to development of atherosclerosis.

Due to analytic challenges in measuring lipoprotein particles, cholesterol and TG assays have served as the basis for estimating lipoprotein concentrations. Hence, plasma TG has come to serve as a surrogate measure of VLDL levels, while LDL cholesterol (LDL-C) and HDL cholesterol (HDL-C) values serves as indicator of the concentrations of LDL and HDL particles.

Data from numerous observational and clinical intervention trials consistently demonstrate a strong relationship between elevated LDL-C levels and increased CHD events. Additionally, reducing high LDL levels with LDL particle lowering agents such as statins significantly reduces CHD risk. Consequently, successive national guidelines have been issued that use LDL-C in conjunction with other established risk factors (e.g., age, gender, blood pressure, HDL-C, diabetes, smoking, and family history) to categorize the patient’s risk and to assign corresponding LDL-C treatment goals. The guiding principle of these guidelines is that the higher the patient’s risk, the lower the LDL-C target needs to be to mitigate that risk. Elevated TG levels are often associated with an increased risk, especially in combination with obesity and other factors.

**Cholesterol Testing**

Traditional cholesterol testing is generally called a lipid profile and determines:

- Total Cholesterol levels,
- LDL levels,
- Total HDL levels,
- Triglyceride levels.
Some routine cholesterol measurements are calculated (i.e., not measured). Most clinical labs do not measure LDL directly as it requires ultracentrifugation which is time consuming, expensive, and requires equipment not commonly available in laboratories. The current standard for determining LDL estimates and CAD risk is the Friedwald equation (1972):

$$\text{LDL} = \text{Total cholesterol (TC) - HDL} - \frac{\text{Triglyceride (TG)}}{5} \text{ (all values in mg/dl), with the quotient TG/5 used as an estimate of VLDL concentration.}$$

**Other Technologies**

The amount of cholesterol and triglyceride carried in various lipoprotein particles is highly variable. As a result, even the most accurate lipid measures may not provide an accurate measurement of lipoprotein particles. Newer technologies are available that allow quantification of LDL particle number, as well as information regarding subclasses of particles that vary by size and density.

Both Nuclear Magnetic Resonance (NMR) technology and the Vertical Auto Profile test (VAP) provide information beyond standard cholesterol values. The NMR LipoProfile test measures the number of particles present in a variety of lipoprotein classes and subclasses including total LDL particle number (LDL-P), small LDL particle number, total HDL particle number (HDL-P), and large HDL particle number. Mean lipoprotein particle sizes of LDL, HDL and VLDL particles are also provided. Multiple outcome trials show a strong and independent relationship of LDL-P with CHD events. The unique value of LDL-P as a measure of LDL quantity is seen when LDL-C and LDL-P results as discordant. When this occurs, CHD risk tracks closely with LDL-P, but not LDL-C. For this reason many expert panels have recommended the use of LDL-P targets (in addition to LDL-C and non-HDL-C) to optimize individual management.

The VAP test categorizes LDL cholesterol and HDL cholesterol by relative size. In this way several LDL and HDL subclasses are reported based on cholesterol content. The VAP test measures some blood lipids that the current lipid profile ignores such as very low density lipoprotein (VLDL); intermediate-density lipoprotein (IDL); and lipoprotein(a) [Lp(a)]. Apolipoprotein B100 (apoB100) is a molecule contained in lipoproteins (Lp(a), LDL, IDL, and VLDL) and measurement of this concentration may represent the total number of atherogenic particles. An estimate of apoB100 can be calculated by knowledge of non-HDL-C and inferred LDL size, although outcome studies using calculated apoB100 have not been reported.

**Society Guidelines**

Data from population and clinical intervention trials consistently demonstrate that elevated LDLC levels are strongly related to increased CHD events, and that reducing high LDL levels with LDL particle–lowering agents, such as statins, significantly reduce CHD risk. In 2001, the Adult Treatment Panel III (ATP III) revised the National Cholesterol Education Program (NCEP) guidelines for detection and treatment of hypercholesterolemia in adults. The guiding principle of the ATP III guidelines is that the higher the patient’s risk, the lower the LDL level needs to be to mitigate that risk.

One limitation of this approach is that the cholesterol content of LDL particles is not constant, varying more than two-fold between individuals. Additionally, the cholesterol content of a given patient’s LDL particles is not fixed, but can change over time in response to lipid-altering treatments. Many studies have evaluated the prevalence and clinical consequences of differences between cholesterol and particle number measures of LDL quantity. Collectively, when LDL particle number is elevated, CHD events are increased. When LDL particle
number is low, CHD events are decreased. If cholesterol (LDL-C and non-HDL-C) and LDL particle number measures are discordant, risk tracks with LDL particle number. As a result, several expert panels including the American College of Cardiology, American Diabetes Association, American Association of Clinical Chemistry, National Lipid Association, and American Association of Clinical Endocrinologists advise treating to LDL particle number targets (either NMR LDL-P or measured Apo B), in addition to LDL-C and non-HDL-C, to optimize management of moderate and high risk individuals.

The U.S. Preventive Services Task Force (USPSTF) has issued a set of recommendations for the screening lipid disorders. For men, the USPSTF strongly recommends screening men 35 years and older for lipid disorders and recommends screening men 20 to 35 years of age for lipid disorders if they are at increased risk of CHD. Likewise for women, she USPSTF strongly recommends screening women 45 years and older for lipid disorders if they are at increased risk of CHD and recommends screening women 20 to 45 years of age for lipid disorders if they are at increased risk of CHD.

The USPSTF makes no recommendation for or against routine screening for lipid disorders in men 20 to 35 years of age, or in women 20 years and older who are not at increased risk of CHD. Additionally, the USPSTF makes no recommendation for or against routine screening for lipid disorders in infants, children, adolescents, or young adults (up to age 20) due to lack of clinical evidence to support screening.

**POLICY**

For the following CPT code(s) in Table 1, the patient should have a diagnosis (ICD-10-CM) code(s) listed in the attached files below.

**Table 1. HCPCS Codes (Alphanumeric, CPT® AMA)**

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tr>
<td>80061</td>
<td>Lipid panel</td>
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<tr>
<td>82465</td>
<td>Cholesterol, serum or whole blood, total</td>
</tr>
<tr>
<td>83700</td>
<td>Lipoprotein, blood; electrophoretic separation and quantitation</td>
</tr>
<tr>
<td>83701</td>
<td>Lipoprotein blood; high resolution fractionation and quantitation of lipoproteins including lipoprotein subclasses when performed (e.g., electrophoresis, ultracentrifugation)</td>
</tr>
<tr>
<td>83704</td>
<td>Quantitation of lipoprotein particle number(s) (eg, by nuclear magnetic resonance spectroscopy), includes lipoprotein particle subclass(es), when performed</td>
</tr>
<tr>
<td>83718</td>
<td>Lipoprotein, direct measurement; high density cholesterol (HDL cholesterol)</td>
</tr>
<tr>
<td>83721</td>
<td>Lipoprotein, direct measurement, LDL cholesterol</td>
</tr>
<tr>
<td>84478</td>
<td>Triglycerides</td>
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**ICD-10 Diagnosis Codes (Proven)**

CMP-012 Lipid Testing ICD10_v1.1
REFERENCES


POLICY HISTORY/REVISION HISTORY

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<tr>
<td></td>
<td>Annual Policy Review Completed – Updated ICD10 codes as per CMS recommendations.</td>
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<tr>
<td>01/21/2017</td>
<td>Updated ICD10 codes as per CMS recommendations. Removed ICD9 code file.</td>
</tr>
<tr>
<td>10/01/2015</td>
<td>Removed ICD9 table. Embedded ICD9/ICD10 PDF files.</td>
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