HOMOCYSTEINE TESTING

Policy Number: CMP - 026
Effective Date: October 1, 2015

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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

Homocysteine, a non-protein amino acid, is used by the body to make protein and to build and maintain tissue. Homocysteine levels in the blood are strongly influenced by diet and genetic factors. Too much homocysteine may increase the risk of stroke, certain types of heart disease, and peripheral arterial disease. Elevated blood levels of homocysteine have also been linked with a wide range of health disorders including stroke, macular degeneration, hearing loss, migraine, brain atrophy, dementia, osteoporosis, and cancer.

Folic acid and other B vitamins help break down homocysteine in the body. Dietary folic acid and vitamins B-6 and B-12 have the greatest effects. Several studies found that higher blood levels of B vitamins are related, at least in part, to lower concentrations of homocysteine. Other evidence shows that low blood levels of folic acid are linked with a higher risk of fatal coronary heart disease and stroke.

Testing for homocysteine may be useful in:
• Diagnosing homocystinuria, vitamin B12 deficiency, and folate deficiency

• Assessing risk of cardiovascular disease (CVD), stroke, and dementia (including Alzheimer’s disease)

• Monitoring therapy in patients with elevated homocysteine levels

**Associated Conditions**

**Risk of Mortality**

Elevated plasma homocysteine level is an independent risk factor for cardiovascular-related as well as non-cardiovascular-related mortality.\(^2\)\(^-\)\(^4\) In a prospective cohort study following 2,127 men and 2,639 women for over 4 years, increasing levels of plasma homocysteine were directly related with increasing mortality.\(^2\)

**Cardiovascular Risks**

A high level of blood serum homocysteine is a powerful risk factor for cardiovascular disease. Evidence suggests that homocysteine may promote atherosclerosis (fatty deposits in blood vessels) by damaging the inner lining of arteries and promoting blood clots.\(^1\)\(^,\)\(^5\)\(^,\)\(^6\) In 1968, a Harvard researcher observed that children with a genetic defect that caused them to have elevated homocysteine levels suffered severe atherosclerotic occlusion and vascular disorders similar to what is seen in older patients with arterial disease.\(^1\) This was the first indication that excess homocysteine might be an independent risk factor for heart disease.\(^1\) Even though, detection of high levels of homocysteine has been linked to cardiovascular disease; lowering homocysteine levels may not improve outcomes.\(^7\)

Heart failure can result from multiple cardiovascular conditions including after an acute myocardial infarction (AMI). Additionally, in multiple clinical studies it has been demonstrated that elevated plasma homocysteine levels may be associated with the development of heart failure.\(^8\)\(^-\)\(^10\) Data from several studies suggests that that homocysteine levels may be better predictors for recurrent cardiovascular events than for primary cardiovascular events.\(^4\)\(^,\)\(^11\) There is also data that suggests that elevated homocysteine is a risk factor for primary hypertension as well as primary pulmonary hypertension.\(^12\)\(^,\)\(^13\)

Homocysteine is also an independent risk factor for ischemic stroke.\(^14\)\(^-\)\(^16\) Increased recurrent stroke based on increasing homocysteine levels has been demonstrated.\(^16\) In a meta-analysis, published in JAMA, the Homocysteine Studies Collaboration analyzed data from 30 prospective and retrospective studies. This meta-analysis suggested that elevated homocysteine is at most a modest independent predictor of IHD and stroke risk in healthy populations.\(^14\)

**Kidney Disorders**

When kidneys are functioning normally, they play a role in the metabolism and filtration of removing homocysteine from the blood. Hyperhomocysteinemia is common among patients with chronic renal insufficiency and end-stage renal disease.\(^17\) This is of importance for the latter group of patients, in with cardiovascular disease is the major cause of death.\(^17\) These patients may have a 30 times higher risk of cardiovascular-related death than the general population.\(^17\)

**Macular Degeneration**
Studies of homocysteine’s role in age-related macular degeneration (AMD: both wet and dry types) reveal a strong link between the compound and the disease.\textsuperscript{18, 19} In a group of 2,335 study participants who had evidence of AMD as detected from retinal photographs, researchers found that elevated homocysteine blood levels were associated with an increased likelihood of AMD in participants aged <75 years.\textsuperscript{18}

**Migraines, Cognitive Disorders and Dementia**

Migraine is a debilitating disease that can be associated with elevated blood levels of homocysteine.\textsuperscript{20-22} Likewise, elevated plasma homocysteine levels have been associated with poor cognition and dementia. In a study of 1092 subjects (from the Framingham Study) without dementia, the subjects were followed for 8 years and the researchers found that 111 subjects developed dementia (including 83 subjects diagnosed with Alzheimer’s disease).\textsuperscript{23} The study, published in the New England Journal of Medicine, concluded that an increased plasma homocysteine level is a strong, independent risk factor for the development of dementia and Alzheimer's disease.\textsuperscript{23}

**Diabetes**

There is no specific causal relationship between the risk of type II diabetes and homocysteine levels; however, they are both independent risk factors for cardiovascular disease.\textsuperscript{24, 25} In a study of diabetic patients with elevated levels of homocysteine, these patients had a 2-fold higher risk of mortality than other diabetic patients.\textsuperscript{24} Additionally, recent study have reported that homocysteine is linked to vaso-occlusive disorders in the eye and the level of plasma homocysteine may be a useful biomarker or a novel risk factor for increased risk of diabetic retinopathy in patients with type 2 DM.\textsuperscript{25}

**Other Conditions**

Numerous other diseases have been linked to elevated homocysteine levels, including deep-vein thrombosis,\textsuperscript{26} neural-tube and other birth defects,\textsuperscript{28, 29} peripheral arterialocclusive disease,\textsuperscript{30, 31} Parkinson’s disease,\textsuperscript{32} and polycystic ovarian disease.\textsuperscript{33, 34}

**POLICY**

BeaconLBS recommends that for the following CPT code(s) in Table 1, the patient should have a diagnosis (ICD-9-CM, ICD-10-CM) code(s) listed in the attached files below.

**Table 1. HCPCS Codes (Alphanumeric, CPT\textsuperscript{\textregistered} AMA)**

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<th>HCPCS Code</th>
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<tr>
<td>83090</td>
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REFERENCES


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**POLICY HISTORY/REVISION HISTORY**

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<th>BLBS Approval Signature Date</th>
<th>Policy Version</th>
<th>Action/Description</th>
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<td></td>
<td>V2.0</td>
<td>Removed ICD9 code table. Replaced with embedded ICD9/ICD10 pdf files.</td>
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