VITAMIN TESTING (VITAMIN B12, FOLATE, CARNITINE, VITAMIN B6)

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Table of Contents

<table>
<thead>
<tr>
<th></th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>BACKGROUND</td>
<td>1</td>
</tr>
<tr>
<td>POLICY</td>
<td>4</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>5</td>
</tr>
<tr>
<td>POLICY HISTORY/REVISION HISTORY</td>
<td>9</td>
</tr>
</tbody>
</table>

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

This background will cover testing for Vitamin B12, folate, carnitine, and vitamin B6.

Vitamin B12

Vitamin B12, also called cobalamin, is one of 8 B vitamins. Vitamin B12, a water-soluble vitamin, is naturally present in some foods, added to others, and available as a dietary supplement and a prescription medication. Vitamin B12 is an important vitamin in red blood cell development, neurological function, and the production of DNA and RNA. Folate and B12 work together to produce compounds involved in immune function and mood. In addition, vitamins B12, B6, and B9 work together to control blood levels of the amino acid homocysteine.

The main causes of vitamin B12 deficiency include vitamin B12 malabsorption from food, pernicious anemia, postsurgical malabsorption, and dietary deficiency. Deficiency of vitamin B12 is often characterized by megaloblastic anemia, fatigue, weakness, constipation, loss of appetite, and weight loss. Other changes such
as numbness and tingling in the hands and feet can also occur. Additional symptoms of vitamin B12 deficiency include difficulty maintaining balance, depression, confusion, dementia, poor memory, and soreness of the mouth or tongue. During infancy, signs of a vitamin B12 deficiency include failure to thrive, movement disorders, developmental delays, and megaloblastic anemia.

Vitamin B12 has the potential to interact with certain medications. In addition, several types of medications including chloramphenicol, proton pump inhibitors, such as omeprazole (Prilosec®) and lansoprazole (Prevacid®), histamine H2 receptor antagonists and metformin might adversely affect vitamin B12 levels.

**Folate**

Vitamin B9, also called folate or folic acid, is one of 8 B vitamins. Folic acid is the synthetic form of B9, found in supplements and fortified foods, while folate occurs naturally in foods. Folate is needed to make DNA and RNA and folate helps prevent changes to DNA that may lead to cancer. Folate is needed to make normal red blood cells and prevent anemia. Also, folate is important in the metabolism of homocysteine, and helps maintain normal levels of this amino acid. During periods of rapid cell growth and division, such as in pregnancy and infancy, folate is an important vitamin. Pregnant women need more folic acid to lower the risk of neural tube birth defects, including cleft palate, spina bifida, and brain damage.

It is common to have low levels of folic acid. Medical conditions that increase the need for folate or result in increased loss of folate include alcoholism, inflammatory bowel disease, celiac disease, kidney dialysis, liver disease, certain anemias, and pregnancy and lactation. Medications that interfere with the metabolism of folate may also increase the need for this vitamin and risk of deficiency. Medications that interfere with folate utilization include anticonvulsants, metformin, sulfasalazine, triamterene, methotrexate, and barbiturates.

Folic acid deficiency can cause poor growth, weight loss, weakness, anemia, headaches, heart palpitations, behavioral disorders, tongue inflammation, gingivitis, loss of appetite, shortness of breath, diarrhea, irritability, forgetfulness, and mental sluggishness. There is also some evidence that associates low blood levels of folate with a greater risk of cancer. As folate is involved in the synthesis, repair, and function of DNA, deficiency of folate can cause damage to DNA that may lead to cancer. Other conditions, including age-related hearing loss, age-related macular degeneration, and depression, may improve with folic acid supplements.

**Carnitine**

Carnitine is found in nearly all cells of the body. Carnitine is produced endogenously in the kidneys and liver and also found in meat and dairy products in the diet. However, healthy children and adults do not need to consume carnitine from food or supplements, as the liver and kidneys generally produce sufficient amounts from the amino acids lysine and methionine to meet daily needs. Carnitine, predominately concentrated in skeletal and cardiac muscle tissues, plays a critical role in energy production and removal of toxic compounds from the mitochondria.

There are two types of carnitine deficiency states that exist – primary or secondary. Primary carnitine deficiency is a genetic disorder of the cellular carnitine-transporter system that usually manifests itself by five years of age. In primary carnitine deficiency, the body is unable to use certain fats for energy particularly during periods without food. Symptoms of primary carnitine deficiency include cardiomyopathy, skeletal-muscle weakness, encephalopathy, confusion, vomiting, and hypoglycemia.
All individuals with this disorder are at risk for heart failure, liver problems, coma, and sudden death. Secondary carnitine deficiencies may occur due to certain disorders (such as chronic renal failure) or under particular conditions (e.g., use of certain antibiotics) that reduce carnitine absorption or increase its excretion.\textsuperscript{38, 39}

Several studies have examined carnitine supplements for the management of cardiac ischemia and peripheral arterial disease.\textsuperscript{40, 41} Because levels of carnitine are low in the failing heart muscle, supplemental amounts might be beneficial to the organ.\textsuperscript{40} Preliminary studies have suggested that supplementation of carnitine in diabetic patients may improve insulin sensitivity.\textsuperscript{42-44} Similarly, supplementing carnitine in HIV-infected patients may slow the death of lymphocytes (which slows the progression of HIV).\textsuperscript{45, 46}

Supplementing with carnitine may protect cells from drugs including HIV medications, chemotherapy medications, and strong anti-acne medications, that have known toxic effects or may have negative interactions.\textsuperscript{47} Carnitine may also stop thyroid hormone from getting into cells, and theoretically may make thyroid hormone replacement less effective.\textsuperscript{47}

Vitamin B6

Vitamin B6, also called pyridoxine, is one of eight B vitamins.\textsuperscript{48} Vitamin B6, a water-soluble vitamin, is naturally present in a variety of foods including fish, fruit, potatoes and other starchy vegetables, and beef live and other organ meats, available in fortified foods or as a supplement.\textsuperscript{7, 49-52} Vitamin B6 helps the body to make antibodies, maintain normal nerve function by making several neurotransmitters, make hemoglobin, metabolize fats and proteins, and convert carbohydrates into glucose to subsequently produce energy.\textsuperscript{7, 48, 49} Along with vitamins B12 and folic acid (B9), vitamin B6 helps control levels of homocysteine in the blood. Homocysteine is an amino acid that may be associated with heart disease.\textsuperscript{48}

Additionally, the body uses vitamin B6 to absorb vitamin B12 in order to red blood cells and cells of the immune system.\textsuperscript{48} While it is rare to have a significant deficiency of B6, studies indicate many people may be mildly deficient, especially children and the elderly.\textsuperscript{48} Symptoms of a deficiency include microcytic anemia, electroencephalographic abnormalities, weakened immune function, muscle weakness, nervousness, irritability, depression, difficulty concentrating, dermatitis with cheilosis (scaling on the lips and cracks at the corners of the mouth), glossitis (swollen tongue), depression and confusion, and short-term memory loss.\textsuperscript{7, 48, 53, 54}

Vitamin B6 deficiency in adults principally affects the peripheral nerves, skin, mucous membranes, and the circulatory system.\textsuperscript{53} In children, the central nervous system is also affected. Individuals with uremia, alcoholism, cirrhosis, hyperthyroidism, malabsorption syndromes, and congestive heart failure (CHF), and in those taking certain medications may suffer from vitamin B6 deficiency.\textsuperscript{7, 49, 54-56}

Vitamin B6 can adversely affect certain medications. It has been documented that vitamin B6 supplementation can reduce serum concentrations of certain drugs (including phenytoin and Phenobarbital) or interfere with the absorption (including tetracycline and levodopa), thereby changing the drugs metabolism.\textsuperscript{48, 57, 58} Vitamin B6 can improve the effectiveness or reduce side effects of some drugs including some tricyclic antidepressants or chemotherapy medications.\textsuperscript{48} Additionally, there are several types of medications including, but not limited to certain antibiotics, anti-epileptics, and asthma medications that affect vitamin B6.\textsuperscript{48, 52, 59, 60}
For the CPT code(s) in the attached files, the patient should have the corresponding diagnosis (ICD-10-CM) code(s).

**ICD-10 Diagnosis Codes (Proven)**

CMP-037 Vitamins
ICD10_v2.3
REFERENCES


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<th>Action/Description</th>
</tr>
</thead>
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<td>01/21/2017</td>
<td>Updated ICD10 codes as per CMS recommendations. Removed ICD9 code file.</td>
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<tr>
<td>12/03/2015</td>
<td>Annual Policy Review Completed – changes made:</td>
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<td>Added ICD9 diagnosis codes related to protein-calorie malnutrition: 751.5</td>
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<tr>
<td></td>
<td>Added ICD10 diagnosis codes related to protein-calorie malnutrition: Q43.4, Q43.5, Q43.6, Q43.7, Q43.8, Q43.9</td>
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<td>10/01/2015</td>
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</tbody>
</table>