Subject: Vitamin B12 Screening & Testing

Background: Vitamin B12 is a water-soluble vitamin that is required for proper red blood cell formation, neurological function, and DNA synthesis. Vitamin B12 is assessed using a serum blood test and is assessed using the following ranges:

- 200-900 pg/mL: Normal
- 200-300 pg/mL: Borderline low
- <200 pg/mL: Low – consistent with vitamin B12 deficiency

Policy and Coverage Criteria:
Harvard Pilgrim Health Care (HPHC) considers routine vitamin B12 screening and testing in healthy, asymptomatic adults not medically necessary.

Harvard Pilgrim Health Care (HPHC) considers Vitamin B12 screening and testing medically necessary for members who are clinically symptomatic or considered high-risk for deficiency due to certain medical conditions, including:

- Abnormalities of gait, mobility, or coordination
- Achlorhydia
- Alcohol dependence
- Alzheimer's disease
- Amnesia
- Anemia
- Anorexia
- Blind loop syndrome
- Celiac disease
- Crohn's disease
- Diabetes mellitus with neuropathy, amyotrophy, or neurologic complication
- Disease of the blood or blood-forming organs
- Disturbances of skin sensation
- Eating disorders
- Endocrine, nutritional, or metabolic disease
- Failure to thrive (child)
- Glossodynia
- Homocystinuria
- Human immunodeficiency virus (HIV) disease
- Hypergammaglobulinemia
- Malabsorption
- Malnutrition
- Marasmus
- Neuropathy
• Osteomyelofibrosis
• Pancreatic steatorrhea
• Pernicious anemia
• Prolonged drug use (i.e., PPI, Metformin)
• Senile dementia
• Sulfur-bearing amino-acid metabolism disorders
• Tropical sprue
• Veganism
• Vitamin deficiency or other B-complex deficiencies
• Whipple’s disease

HPHC considers the testing of methylmalonic acid (MMA) medically necessary for the diagnosis of vitamin B12 deficiency when vitamin B12 levels are borderline-low or low.

HPHC considers the testing of holo-transcobalamin as a marker of vitamin B12 investigational/experimental.

Exclusions:
Vitamin B12 screening and testing for conditions not listed above. MMA testing in the absence of a low vitamin B12 result.

Supporting Information:
Vitamin B12 (cobalamin) is a water-soluble vitamin that is required for proper red blood cell formation, neurological function, and DNA synthesis. Animal products are the only natural dietary source of cobalamin for humans. Dietary cobalamin binds to R factors in the presence of acid and pepsin in the stomach after being liberated from its binding to protein. Cobalamin is then freed from the R proteins in the duodenum by pancreatic proteases then binds to intrinsic factor. Adequate absorption of cobalamin is dependent on the following factors: adequate dietary intake, acid-pepsin present in the stomach, intrinsic factor secretion, and an intact ileum with functional Cbl-IF receptors. The Institute of Medicine has not assigned an upper limit for cobalamin intake due to the low risk for toxicity and lack of adverse effects associated with excess intake from food or supplements. Vitamin B12 deficiency is typically caused by inadequate absorption due to pernicious anemia, however, there are numerous potential causes for a B12 deficiency. Serum vitamin B12 levels show high sensitivity for deficiency but have low specificity. Oral contraceptive use and pregnancy can falsely lower serum B12 levels, increasing the risk for over diagnosis and mistreatment. Methylmalonic acid is a dicarboxylic acid naturally found in the blood. When serum vitamin B12 levels are low or borderline-low, plasma MMA concentrations are elevated. Testing plasma MMA concentrations may be useful to confirm vitamin B12 deficiency.

The U.S. Preventive Services Task Force does not currently have published guidelines on screening asymptomatic adults for vitamin B12 deficiency. There are no current guidelines or recommendations related to routine testing of cobalamin. Recommendations for testing are condition or symptom specific. The Medical Service Commission of Canada states that routine screening for cobalamin deficiency is not indicated. The Centers for Medicare & Medicaid Services also do not provide coverage for routine testing for vitamin B12 deficiency. There is agreement within the literature that serum vitamin B12 testing should be used to diagnose vitamin B12 deficiency in symptomatic and high-risk populations.
One of the leading causes of vitamin B12 deficiency is pernicious anemia, an autoimmune disease that results in the failure to produce intrinsic factor. Other common causes of vitamin B12 deficiency include gastric and intestinal disorders effecting absorption, veganism, alcoholism, and metabolism disorders.

The main characteristics of vitamin B12 deficiency include megaloblastic anemia, fatigue, weakness, constipation, loss of appetite, weight loss and neurological changes. Common symptoms associated with deficiency include difficulty with gait and balance, depression, confusion, dementia, impaired memory, and mouth and tongue soreness. Populations who are most at risk for deficiency include older adults, individuals with pernicious anemia, individuals with gastrointestinal disorders, individuals who have undergone bariatric surgery, and strict vegetarians/vegans.

CMS: Vitamin or micronutrient testing may not be used for routine screening. Once a beneficiary has been shown to be vitamin deficient, further testing is medically necessary only to ensure adequate replacement has been accomplished. Thereafter, annual testing may be appropriate depending upon the indication and other mitigating factors. Utilization Guidelines: Vitamin B-12 (82607) can be tested up to four times per year for malabsorption syndromes (579.9) or deficiency disorders (266.2, 281.1 and 281.2). Vitamin B-12 (82607) can only be tested more frequently than four times per year for postsurgical malabsorption (579.3).

AAFP: the U.S. Preventive Services Task Force does not have published guidelines on screening asymptomatic adults for vitamin B12 deficiency.

MSC: Routine screening for cobalamin deficiency is not indicated. Testing should be done in individuals with unexplained neurologic symptoms, such as paresthesias, numbness, poor motor concentration, memory lapses or cognitive and personality changes. Testing should also be done in individuals with macrocytic anemia or macrocytosis with oval or hypersegmented neutrophils or pancytopenia. Testing should be considered in the elderly, individuals with a history of inflammatory bowel disease, individuals with a history of gastric or intestine resection, individuals who follow a prolonged vegan diet, individuals with long-term use of H2 receptor antagonists or proton pump inhibitors (at least 12 months), or metformin (at least 4 months).

Coding:
Codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible.

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>82607</td>
<td>Cyanocobalamin (Vitamin B12)</td>
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<tr>
<td>84999</td>
<td>Unlisted chemistry procedure [not covered when billed for holo-transcobalamin as a marker of vitamin B12]</td>
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List of medically necessary ICD-10 Codes

Billing Guidelines:
Member’s medical records must document that services are medically necessary for the care provided. Harvard Pilgrim Health Care maintains the right to audit the services provided to our members, regardless of the participation status of the provider. All documentation must be available to HPHC upon request. Failure to produce the requested information may result in denial or retraction of payment.

References:


HPHC Clinical Medical Policy

Vitamin B12 Screening and Testing

HPHC policies are based on medical science, and written for the majority of people with a given condition.

Coverage described in this policy is standard under most HPHC plans. Specific benefits may vary by product and/or employer group. Please reference appropriate member materials (e.g., Benefit Handbook, Certificate of Coverage) for member-specific benefit information.
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Summary of Changes

<table>
<thead>
<tr>
<th>Date</th>
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<tbody>
<tr>
<td>9/17</td>
<td>Coding Update</td>
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<tr>
<td>4/16</td>
<td>Clarifies medical necessity. ICD codes updated</td>
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Approved by UMCPC: 9/13/17
Reviewed/Revised: 4/16; 9/17