



Medical Policy

Vitamin B12 Testing

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Policy Number: 061

BCBSA Reference Number: N/A

NCD/LCD: N/A

Related Policies

- Vitamin D Assay Testing, #[746](#)

Policy¹

**Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO BlueSM and Medicare PPO BlueSM Members**

VITAMIN B12 TESTING

Measurement of Vitamin B12 level is considered [MEDICALLY NECESSARY](#) for individuals with **any** of the following indications:

- Inadequate intake of B12 (Malnutrition)
 - Alcohol dependence
 - Eating disorders (e.g. Anorexia)
 - Inadequate dietary intake of vitamin B12 such as strict vegan diet without vitamin B12 supplementation.
- Insufficient absorption of B12 (Malabsorption)
 - Achlorhydria
 - Blind loop syndrome
 - Celiac disease
 - Chronic use of H2 blocker or proton pump inhibitor (PPI) (minimum of 1 year)
 - Crohn's disease
 - Disruption of gastrointestinal anatomy or function (for example achlorhydria, gastrectomy, gastric bypass, gastric cancer, ileal resection, inflammatory bowel disease)
 - Infection known to be associated with vitamin B12 deficiency such as bacterial overgrowth syndrome, fish tapeworm infection, Helicobacter pylori infection, or human immunodeficiency virus (HIV)
 - Malignancy affecting absorption of nutrients
 - Pancreatic insufficiency/pancreatic steatorrhea.

- Pernicious anemia/intrinsic factor deficiency
- Tropical sprue
- Whipple's disease.
- Metabolic causes
 - Disorders of sulphur amino acid metabolism Homocystinuria
 - Methylene tetrahydrofolate Reductase (MTHFR) deficiency
 - Chronic use of metformin (minimum of 4 months).
- Symptoms suggesting B12 deficiency
 - Abnormalities of gait, mobility, or coordination
 - Alzheimer's disease
 - Amnesia
 - Anemia and other cytopenias/dyscrasias Osteomyelofibrosis
 - Diabetes mellitus with neuropathy, amyotrophy, or neurologic complication
 - Disturbances of skin sensation
 - Failure to thrive (pediatric)
 - Glossitis/Glossodynia
 - Marasmus
 - Neurologic or motor symptom abnormality
 - Neuropathy
 - Unexplained mental status or cognitive changes.

Vitamin B12 screening and testing is considered **NOT MEDICALLY NECESSARY** for all other indications.

METHYLMALONIC ACID TESTING

Methylmalonic acid (MMA) testing is considered **MEDICALLY NECESSARY** for ANY of the following indications:

- Vitamin B12 levels are low or borderline-low; or
- Positive newborn screening suggesting organic acidemia; or
- Metformin use for Type 2 diabetes mellitus with neurologic symptoms.

Vitamin B12 and MMA testing is considered **NOT MEDICALLY NECESSARY** for all other indications.

HOLOTRANSCOBALAMIN TESTING

Holotranscobalamin testing as a marker for vitamin B12 deficiency is considered **INVESTIGATIONAL** for all indications.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is <u>not required</u> .
Commercial PPO and Indemnity	Prior authorization is <u>not required</u> .
Medicare HMO Blue	Prior authorization is <u>not required</u> .
Medicare PPO Blue	Prior authorization is <u>not required</u> .

CPT Codes / HCPCS Codes / ICD Codes

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The above medical necessity criteria **MUST** be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
82607	Cyanocobalamin (Vitamin B-12);

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT code above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM diagnosis codes:	Code Description
B20	Human immunodeficiency virus [HIV] disease
B70.0	Diphyllobothriasis
B96.81	Helicobacter pylori [H. pylori] as the cause of diseases classified elsewhere
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
D51.0	Vitamin B12 deficiency anemia due to intrinsic factor deficiency
D51.1	Vitamin B12 deficiency anemia due to selective vitamin B12 malabsorption with proteinuria
D51.3	Other dietary vitamin B12 deficiency anemia
D51.8	Other vitamin B12 deficiency anemias
D51.9	Vitamin B12 deficiency anemia, unspecified
D53.0	Protein deficiency anemia
D53.1	Other megaloblastic anemias, not elsewhere classified
D53.8	Other specified nutritional anemias
D53.9	Nutritional anemia, unspecified
D64.9	Anemia, unspecified
E10.40	Type 1 diabetes mellitus with diabetic neuropathy, unspecified
E10.43	Type 1 diabetes mellitus with diabetic autonomic (poly)neuropathy
E10.44	Type 1 diabetes mellitus with diabetic amyotrophy
E10.49	Type 1 diabetes mellitus with other diabetic neurological complication

E11.40	Type 2 diabetes mellitus with diabetic neuropathy, unspecified
E11.43	Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy
E11.44	Type 2 diabetes mellitus with diabetic amyotrophy
E11.49	Type 2 diabetes mellitus with other diabetic neurological complication
E13.4	Other specified diabetes mellitus with neurological complications
E41	Nutritional marasmus
E53.8	Deficiency of other specified B group vitamins
E53.9	Vitamin B deficiency, unspecified
E63.9	Nutritional deficiency, unspecified
E72.10	Disorders of sulfur-bearing amino-acid metabolism, unspecified
E72.11	Homocystinuria
E72.12	Methylenetetrahydrofolate reductase deficiency
E72.19	Other disorders of sulfur-bearing amino-acid metabolism
E83.01	Wilson's disease
F10.20	Alcohol dependence, uncomplicated
F10.21	Alcohol dependence, in remission
F10.220	Alcohol dependence with intoxication, uncomplicated
F10.221	Alcohol dependence with intoxication delirium
F10.229	Alcohol dependence with intoxication, unspecified
F10.230	Alcohol dependence with withdrawal, uncomplicated
F10.231	Alcohol dependence with withdrawal delirium
F10.232	Alcohol dependence with withdrawal with perceptual disturbance
F10.239	Alcohol dependence with withdrawal, unspecified
F10.24	Alcohol dependence with alcohol-induced mood disorder
F10.250	Alcohol dependence with alcohol-induced psychotic disorder with delusions
F10.251	Alcohol dependence with alcohol-induced psychotic disorder with hallucinations
F10.259	Alcohol dependence with alcohol-induced psychotic disorder, unspecified
F10.26	Alcohol dependence with alcohol-induced persisting amnestic disorder
F10.27	Alcohol dependence with alcohol-induced persisting dementia
F10.280	Alcohol dependence with alcohol-induced anxiety disorder
F10.281	Alcohol dependence with alcohol-induced sexual dysfunction
F10.282	Alcohol dependence with alcohol-induced sleep disorder
F10.288	Alcohol dependence with other alcohol-induced disorder
F10.29	Alcohol dependence with unspecified alcohol-induced disorder
F50.00	Anorexia nervosa, unspecified
F50.010	Anorexia nervosa, restricting type, mild
F50.011	Anorexia nervosa, restricting type, moderate
F50.012	Anorexia nervosa, restricting type, severe
F50.013	Anorexia nervosa, restricting type, extreme
F50.014	Anorexia nervosa, restricting type, in remission
F50.019	Anorexia nervosa, restricting type, unspecified
F50.020	Anorexia nervosa, binge eating/purging type, mild
F50.021	Anorexia nervosa, binge eating/purging type, moderate
F50.022	Anorexia nervosa, binge eating/purging type, severe
F50.023	Anorexia nervosa, binge eating/purging type, extreme
F50.024	Anorexia nervosa, binge eating/purging type, in remission
F50.029	Anorexia nervosa, binge eating/purging type, unspecified
F50.20	Bulimia nervosa, unspecified
F50.21	Bulimia nervosa, mild
F50.22	Bulimia nervosa, moderate
F50.23	Bulimia nervosa, severe

F50.24	Bulimia nervosa, extreme
F50.25	Bulimia nervosa, in remission
F50.810	Binge eating disorder, mild
F50.811	Binge eating disorder, moderate
F50.812	Binge eating disorder, severe
F50.813	Binge eating disorder, extreme
F50.814	Binge eating disorder, in remission
F50.819	Binge eating disorder, unspecified
F50.84	Rumination disorder in adults
F50.82	Avoidant/restrictive food intake disorder
F50.89	Other specified eating disorder
F50.9	Eating disorder, unspecified
F95.2	Tourette's disorder
G10	Huntington's disease
G20.A1	Parkinson's disease without dyskinesia, without mention of fluctuations
G20.A2	Parkinson's disease without dyskinesia, with fluctuations
G20.B1	Parkinson's disease with dyskinesia, without mention of fluctuations
G20.B2	Parkinson's disease with dyskinesia, with fluctuations
G20.C	Parkinsonism, unspecified
G21.8	Other secondary parkinsonism
G21.9	Secondary parkinsonism, unspecified
G24.3	Spasmodic torticollis
G24.8	Other dystonia
G24.9	Dystonia, unspecified
G25.0	Essential tremor
G25.1	Drug-induced tremor
G25.2	Other specified forms of tremor
G25.3	Myoclonus
G25.4	Drug-induced chorea
G25.5	Other chorea
G30.0	Alzheimer's disease with early onset
G30.1	Alzheimer's disease with late onset
G30.8	Other Alzheimer's disease
G30.9	Alzheimer's disease, unspecified
G90.3	Multi-system degeneration of the autonomic nervous system
K14.0	Glossitis
K14.6	Glossodynia
K31.83	Achlorhydria
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication

K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.40	Inflammatory polyps of colon without complications
K51.411	Inflammatory polyps of colon with rectal bleeding
K51.412	Inflammatory polyps of colon with intestinal obstruction
K51.413	Inflammatory polyps of colon with fistula
K51.414	Inflammatory polyps of colon with abscess
K51.418	Inflammatory polyps of colon with other complication
K51.419	Inflammatory polyps of colon with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications

K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications
K90.0	Celiac disease
K90.1	Tropical sprue
K90.2	Blind loop syndrome, not elsewhere classified
K90.81	Whipple's disease
K90.89	Other intestinal malabsorption
K90.9	Intestinal malabsorption, unspecified
K91.1	Postgastric surgery syndromes
K91.2	Postsurgical malabsorption, not elsewhere classified
K91.30	Postprocedural intestinal obstruction, unspecified as to partial versus complete
K91.31	Postprocedural partial intestinal obstruction
K91.32	Postprocedural complete intestinal obstruction
K91.81	Other intraoperative complications of digestive system
K91.82	Postprocedural hepatic failure
K91.83	Postprocedural hepatorenal syndrome
K91.850	Pouchitis
K91.858	Other complications of intestinal pouch
K91.89	Other postprocedural complications and disorders of digestive system
M62.50	Muscle wasting and atrophy, not elsewhere classified
R20.0	Anesthesia of skin
R20.1	Hypoesthesia of skin
R20.2	Paresthesia of skin
R20.8	Other disturbances of skin sensation
R20.9	Unspecified disturbances of skin sensation
R26.0	Ataxic gait
R26.1	Paralytic gait
R26.2	Difficulty in walking, not elsewhere classified
R26.81	Unsteadiness on feet
R26.89	Other abnormalities of gait and mobility
R26.9	Unspecified abnormalities of gait and mobility
R27.0	Ataxia, unspecified
R27.8	Other lack of coordination
R27.9	Unspecified lack of coordination
R41.1	Anterograde amnesia
R41.2	Retrograde amnesia
R41.3	Other amnesia
R41.82	Altered mental status, unspecified
R41.89	Other symptoms and signs involving cognitive functions and awareness
R62.51	Failure to thrive (child)

R71.8	Other abnormality of red blood cells
Z13.21	Encounter for screening for nutritional disorder
Z79.84	Long term (current) use of oral hypoglycemic drugs
Z90.3	Acquired absence of stomach [part of]
Z90.49	Acquired absence of other specified parts of digestive tract
Z98.84	Bariatric surgery status

Description

Vitamin B12

Vitamin B12, also known as cobalamin, is an essential water-soluble vitamin that is needed to form red blood cells, required for DNA synthesis, and aids in proper neurological function. Vitamin B12 is necessary for the development, myelination, and proper function of the central nervous system, hematopoietic cell formation, DNA synthesis, and also serves as cofactor for 2 enzymes. Vitamin B12 is found naturally in animal products, such as fish, meat, eggs, poultry, and dairy or artificially as cyanocobalamin found in supplements.

Risk factors for vitamin B12 deficiency include dietary deficiency, decreased absorption, autoimmune conditions, genetic conditions, or prolonged use of certain medications such as metformin or proton pump inhibitors. Deficiency symptoms in adults may lead to nerve damage, neurologic changes, depression, difficulty maintaining balance, and anemia. Vitamin B12 deficiency in the pediatric population include failure to thrive, developmental delays, movement disorders, and megaloblastic anemia.

Currently there are no guidelines or recommendations related to routine testing of vitamin B12 in asymptomatic adults. The Centers for Medicare & Medicaid Services does not provide coverage for routine testing for vitamin B12 deficiency.

There are 2 forms of supplemental vitamin B12: cyanocobalamin and hydroxocobalamin.

Cyanocobalamin is the only vitamin B12 preparation available in the United States and can be administered orally or parenterally. Tablets of up to 5,000 mcg may be obtained over the counter without a prescription. Parenteral formulations are administered by the provider. Diverse recommendations exist for initial and maintenance vitamin B12 therapy.

Methylmalonic acid (MMA)

Methylmalonic acid (MMA) is a small water-soluble organic acid. As protein gets digested in the gastrointestinal tract small amounts of MMA are created. When vitamin B12 levels are low the enzyme that controls MMA production is blocked, therefore leading to an increase in MMA levels. MMA testing is useful as a confirmation test of vitamin B12 deficiency.

Holotranscobalamin

Holotranscobalamin is the biologically active form of vitamin B12 (cobalamin). Cobalamin in the blood binds to two proteins, transcobalamin and haptocorrin. The Transcobalamin-cobalamin complex is called holotranscobalamin, or holoTC. The holoTC complex functions to transport cobalamin from the terminal ileum to receptors throughout the body.

Summary

Vitamin B12 Testing

For individuals who are at average risk of deficiency cobalamin testing is not recommended. Vitamin B12 deficiency testing is recommended in symptomatic and high-risk populations. For individuals with unexplained neurologic symptoms, such as paresthesias, numbness, poor motor concentration, memory lapses or cognitive and personality changes, testing should be done. Testing should also be done in individuals with macrocytic anemia or macrocytosis with oval or hypersegmented neutrophils or pancytopenia.

For individuals with a history of inflammatory bowel disease, individuals with a history of gastric or intestinal 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), and in elderly populations, vitamin B12 deficiency testing should be considered.

Methylmalonic acid (MMA) Testing

Methylmalonic acid (MMA) testing is helpful as a confirmation test of vitamin B12 deficiency. In asymptomatic high-risk individuals, who have a normal to low-normal serum vitamin B12, MMA testing is appropriate. MMA testing is also useful as a screening tool in newborns to detect inborn errors of metabolism and for detecting vitamin B12 deficiency in Type II diabetic individuals with peripheral neuropathy.

Holotranscobalamin Testing

Holotranscobalamin (holoTC) testing assesses levels of transcobalamin circulating in the blood. Published literature includes comparison studies, case reports, and review articles. There are no published guidelines suggesting holoTC testing should be used in addition, or in place of, total vitamin B12 serum testing.

A study was done in 2021, published by Rothen, to determine the best testing strategies for vitamin B12 deficiency. This secondary data analysis evaluated testing vitamin B12 alone, holoTC alone, both vitamin B12 and holoTC, and reflex testing of holoTC when vitamin B12 levels were in a designated gray zone value range. Rothen et. al found that the diagnostic strategies of determining vitamin B12 deficiency were often predetermined by the laboratories performing the testing. Often the laboratories do not indicate the analytical method used. There is currently no consensus on the best diagnostic strategy for definitive vitamin B12 deficiency testing. Rothen et.al determined if vitamin B12 deficiency is suspected based on neurological or hematological clinical features, then treatment should be initiated, even with normal to low-normal vitamin B12 values.

Policy History

Date	Action
10/2024	Clarified coding information.
2/2024	Clarified coding information.
12/2023	New medical policy describing medically necessary and not medically necessary indications. Effective 12/1/2023.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

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Vitamin B12 testing

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Holotranscobalamin

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Endnotes

¹ Based on expert opinion