

09-J0000-10

[Original Effective Date:](#) 03/15/01

[Reviewed:](#) 03/13/13

[Revised:](#) 11/01/15

Subject: Vitamin B-12 Injections

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Position Statement	Dosage/Administration	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		Decision Tree

DESCRIPTION:

Cyanocobalamin, or vitamin B12, is a B-vitamin. Although cyanocobalamin and vitamin B12 are terms used interchangeably, vitamin B12 is also available as hydroxocobalamin, a less commonly prescribed drug product. Cyanocobalamin is available nasally, orally, and parenterally, and is equal in biologic activity to hydroxocobalamin. Vitamin B12 is found in a variety of foods such as fish, shellfish, meats, and dairy products. Cyanocobalamin is used to treat pernicious anemia and vitamin B12 deficiency, as well as to determine vitamin B12 absorption in the Schilling test. Vitamin B12 is an essential vitamin found in the foods such as meat, eggs, and dairy products. Deficiency in healthy individuals is rare; the elderly, strict vegetarians (i.e., vegan), and members with malabsorption problems are more likely to become deficient. If vitamin B12 deficiency is not treated with a vitamin B12 supplement, then anemia, intestinal problems, and irreversible nerve damage may occur. Oral therapy is not always effective, as some persons lack intrinsic factor, an endogenous substance produced by the stomach and necessary for oral B12 absorption. Other members may not be able to absorb oral vitamin B12 due to surgical removal or dysfunction of the intestines in the area where absorption of vitamin B12 occurs. Thus, parenteral or nasal therapy may be needed; however, intranasal therapy should only be instituted for maintenance treatment after control of the condition has been obtained by the parenteral route.

POSITION STATEMENT:

Vitamin B-12 injections **meet the definition of medical necessity** when used for the treatment of Vitamin B-12 deficiencies as evidenced by a low serum B-12 or by documentation of a condition that causes or is caused by a low serum B-12.

Indications for administration of Vitamin B-12 include:

1. Anemias associated with vitamin B-12 deficiency, as evidenced by [macrocytosis](#), low serum B-12, or abnormal [Schilling test](#):
 - Anemias resulting from prior gastrectomy
 - [Fish tapeworm anemia](#)
 - Macrocytic megaloblastic anemias resulting from gastrointestinal disorders
2. Conditions associated with decreased production of intrinsic factor:
 - [Pernicious anemia](#)
3. Gastrointestinal disorders:
 - Anemia resulting from small bowel resections, strictures, or [blind loop syndrome](#)
 - Malabsorption syndromes (e.g., [sprue](#), idiopathic [steatorrhea](#))
4. [Neuropathies](#) secondary to vitamin B-12 deficiency:
 - Acute phase exacerbation due to malnutrition or alcoholism
 - Combined system degeneration (lateral sclerosis)
5. [Dementia](#) associated with vitamin B-12 deficiency
6. Administered as an adjunct to [Alimta®](#)
7. Administered as an adjunct to [Folotyn™](#)

DOSAGE AND ADMINISTRATION

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Addison's Pernicious Anemia

- Parenteral therapy required for life.
- Administer 100 mcg daily for 6 or 7 days by IM or deep SC injection.
- If there is clinical improvement and a reticulocyte response, give the same amount on alternate days for 7 doses, then every 3 to 4 days for another 2 to 3 weeks; then 100 mcg monthly for life.

Schilling Test

- Flushing dose of 1000 mcg IM.

Alimta® Adjunct

- Member must receive one IM injection of vitamin B-12 during the week preceding the 1st dose of Alimta and every 3 cycles thereafter.
- Subsequent injections may be given the same day as Alimta.

- In clinical trials 1000 mcg was the dose given.

Folotyn™ Adjunct

- Member should receive a vitamin B12 (1 mg) intramuscular no more than 10 weeks prior to first dose of Folotyn™ and every 8 to 10 weeks thereafter.
- Subsequent injections may be given the same day as treatment with Folotyn™.

PRECAUTIONS:

Leber disease: Members with early Leber disease (hereditary optic nerve atrophy) who were treated with cyanocobalamin suffered severe and swift optic atrophy.

Hypokalemia: Hypokalemia and sudden death may occur in severe megaloblastic anemia, which is treated intensely.

Vitamin B12 deficiency: Vitamin B12 deficiency that is allowed to progress for longer than 3 months may produce permanent degenerative lesions of the spinal cord. Doses of folic acid higher than 0.1 mg/day may result in hematologic remission in members with vitamin B12 deficiency. Neurologic manifestations will not be prevented with folic acid, and, if not treated with vitamin B12, irreversible damage will result.

Folate deficiency: Doses of cyanocobalamin exceeding 10 mcg daily may produce hematologic response in members with folate deficiency. Indiscriminate administration may mask the true diagnosis.

Stomach carcinoma: Members with pernicious anemia have about 3 times the incidence of carcinoma of the stomach as the general population, so perform appropriate tests for this condition when indicated.

Hypersensitivity reactions: Anaphylactic shock and death have been reported after parenteral vitamin B12 administration. An intradermal test dose is recommended before cyanocobalamin is administered to patients suspected of being sensitive to the drug.

Renal function impairment: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that members with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at more than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with CNS and bone toxicity. Tissue loading may occur at even lower rates of administration.

Carcinogenesis: Long-term studies in animals to evaluate carcinogenic potential have not been done. There is no evidence from long-term use in members with pernicious anemia that cyanocobalamin is carcinogenic. Pernicious anemia is associated with an increased incidence of carcinoma of the stomach, but this is believed to be related to the underlying pathology and not to treatment with cyanocobalamin.

Children: This product contains benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal "gasping syndrome" in premature infants.

BILLING/CODING INFORMATION:

The following codes may be used for reporting Vitamin B-12 therapy:

HCPCS Coding:

J3420	Injection, Vitamin B-12 cyanocobalamin, up to 1000 mcg
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ICD-10 Diagnosis Codes That Support Medical Necessity:

B70.0	Diphyllobothriasis
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
D52.0	Dietary folate deficiency anemia
D52.1	Drug-induced folate deficiency anemia
D52.8	Other folate deficiency anemias
D52.9	Folate deficiency anemia, unspecified
D53.1	Other megaloblastic anemias, not elsewhere classified
D53.9	Nutritional anemia, unspecified
E40	Kwashiorkor
E41	Nutritional marasmus
E43	Unspecified severe protein-calorie malnutrition
E44.1	Mild protein-calorie malnutrition
E45	Retarded development following protein-calorie malnutrition
E46	Unspecified protein-calorie malnutrition
E53.8	Deficiency of other specified B group vitamins
F02.80	Dementia in other diseases classified elsewhere, without behavioral disturbance

F02.81	Dementia in other diseases classified elsewhere, with behavioral disturbance
G32.0	Subacute combined degeneration of spinal cord in diseases classified elsewhere
G63	Polyneuropathy in diseases classified elsewhere
K29.40	Chronic atrophic gastritis without bleeding
K29.50	Unspecified chronic gastritis without bleeding
K86.1	Other chronic pancreatitis
K90.0	Celiac disease
K90.1	Tropical sprue
K90.2	Blind loop syndrome, not elsewhere classified
K90.3	Pancreatic steatorrhea
K90.4	Malabsorption due to intolerance, not elsewhere classified
K90.89	Other intestinal malabsorption
K90.9	Intestinal malabsorption, unspecified
K91.1	Postgastric surgery syndromes
K91.2	Postsurgical malabsorption, not elsewhere classified
T36.0x5A – T50.z95A	Poisoning by, adverse effect of and underdosing, initial encounter
T36.0x5D – T50.z95D	Poisoning by, adverse effect of and underdosing, subsequent encounter
T36.0x5S – T50.z95S	Poisoning by, adverse effect of and underdosing, sequela

REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products:

National Coverage Determination (NCD) for VITAMIN B12 Injections to Strengthen Tendons, Ligaments, etc., of the Foot (150.6)

Effective Date of this Version

This is a longstanding national coverage determination. The effective date of this version has not been posted.

Benefit Category

Drugs and Biologicals

Note: This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

Indications and Limitations of Coverage

Vitamin B12 injections to strengthen tendons, ligaments, etc., of the foot are **not covered** under Medicare because (1) there is no evidence that vitamin B12 injections are effective for the purpose of strengthening weakened tendons and ligaments, and (2) this is nonsurgical treatment under the subluxation exclusion. Accordingly, vitamin B12 injections **are not considered reasonable and necessary** within the meaning of §1862(a)(1) of the Act.

Cross Reference

Also see the Medicare Benefit Policy Manual, Chapter 1 §30, and Chapter 16 §100.

Local Coverage Determination (LCD): Vitamin B 12 Injections (L33967)

Original Determination Effective Date

For services performed on or after 02/02/2009

Revision Effective Date

For services performed on or after 04/06/2010

Vitamin B 12 is essential for the formation of red blood cells and is used in the treatment of diseases in which there is defective red cell formation.

Vitamin B 12 administration by injection is a covered benefit accepted as **medically necessary** when the beneficiary has a history of a low serum B 12 or conditions causing or caused by a low serum B 12.

In addition, vitamin B 12 will be considered **medically necessary** when administered as an adjunct to Alimta® or Folutyn™ treatment as follows:

- For Alimta® members, members must receive one intramuscular injection of vitamin B 12 during the week preceding the first dose of Alimta® and every three cycles thereafter
- For Folutyn™ members, supplement members with vitamin B 12 1 mg intramuscularly no more than 10 weeks prior to the first dose of Folutyn™, and every 8-10 weeks thereafter
- Subsequent vitamin B 12 injections may be given the same day as either Alimta® or Folutyn™

Vitamin B 12 injections (J3420) used to strengthen tendons, ligaments, etc. of the foot are considered investigational and are therefore noncovered.

DEFINITIONS:

Alimta®: also known as pemetrexed disodium, an antifolate that exerts its antineoplastic activity by disrupting folate-dependent metabolic processes essential for cell replication. It is indicated for the treatment of malignant pleural mesothelioma and non-small cell lung cancer.

Atrophic gastritis: chronic gastritis with atrophy (wasting away) of the mucous membranes and glands.

Bind loop syndrome: syndrome resulting from alterations in the anatomy of the small intestine, as by strictures or after surgery, in which a loop is disconnected from the main stream or when intestinal contents may gain access to it but not readily egress from it; it is associated with bacterial overgrowth, particularly anaerobic organisms, resulting in malabsorption of vitamin B-12, steatorrhea, and anemia.

Celiac disease: a malabsorption syndrome precipitated by the ingestion of gluten-containing foods; affects both children and adults; hereditary factor has been implicated; characterized by diarrhea with bulky, frothy, fatty stools; abdominal distention; flatulence, weight loss, vitamin deficiencies (B, D, and K), electrolyte depletion. Infantile form is marked by irritability, loss of appetite, weakness, extreme wasting, growth retardation, and celiac crisis; adult form is marked by extreme fatigue, difficulty in breathing, clubbing of the fingers, bone pain, cramping of the muscles, tetany, daytime abdominal distention, megacolon, and skin pigmentation.

Dementia: organic mental disorder characterized by loss of intellectual ability involving impaired memory and judgment, abstract thinking as well as personality changes; resulting from a large number of conditions, including pernicious anemia and folic acid deficiency.

Fish tapeworm anemia: pernicious-like anemia resulting from ingestion of raw or undercooked infected fish; although fish tapeworm infection is usually asymptomatic, mild GI symptoms may be noted.

Folotyn™: Also known as pralatrexate is an anti-folate (i.e., a folate analogue metabolic inhibitor) designed to accumulate preferentially in cancer cells.

Hydroxocobalamin: is a natural form of vitamin B12, a basic member of the cobalamin family of compounds. Hydroxocobalamin is the form of vitamin B12 produced by many bacteria which are used to produce the vitamin commercially. Like other forms of vitamin B12, hydroxocobalamin has an intense red color. It is not a form normally found in the human body, but is easily converted in the body to usable coenzyme forms of vitamin B12.

Kwashiorkor: syndrome occurring mainly in the tropics and subtropics which is produced by severe protein deficiency; characterized by retarded growth, changes in skin and hair pigment, edema, and pathologic changes in the liver, including fatty infiltration, necrosis, and fibrosis. Other findings include peevish mental apathy, atrophy of the pancreas, GI disorders, anemia, low serum albumin, and dermatoses.

Macrocytosis: condition where the erythrocytes are larger than normal.

Marasmus, nutritional: marasmic (dying away) kwashiorkor.

Mononeuritis: disease of a single nerve.

Neuritis: inflammation of a nerve or group of nerves, characterized by pain, loss of reflexes, and atrophy of the affected muscle.

Neuropathies: a general term indicating functional disturbances and/or pathological changes in the peripheral nervous system.

Optic neuritis: inflammation of the optic nerve; it may affect the part of the nerve within the eyeball or the portion behind the eyeball.

Paralytic strabismus: that which is due to paralysis of an eye muscle (deviation of the eye which the member cannot overcome).

Pernicious anemia: anemia occurring in children but more commonly in later life, resulting from malabsorption of vitamin B-12 due to a failure of the gastric mucosa to secrete adequate and potent intrinsic factor (also called Addison's anemia, Addison-Biermer anemia, cytogenic anemia, malignant anemia).

Schilling test: a measured amount of radioactive vitamin B-12 is given orally, followed by a parenteral flushing dose of the non-radioactive vitamin, and the percentage of radioactivity is determined in the urine excreted over a 24-hour period.

Sprue: a chronic form of malabsorption syndrome occurring in both tropical and non-tropical forms; tropical sprue occurs in the tropics and subtropics where protein malnutrition is usually precipitated by the malabsorption and anemia due to folic acid deficiency is particularly common.

Steatorrhea: excessive amounts of fat in the feces; associated with malabsorption syndromes.

RELATED GUIDELINES:

[Pemetrexed Disodium \(Alimta®\) IV, 09-J1000-01](#)

[Pralatrexate \(Folotyn™\) IV, 09-J1000-18](#)

OTHER:

None applicable.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Pharmacy Policy Committee on 03/13/13.

GUIDELINE UPDATE INFORMATION:

03/15/01	Medical Coverage Guideline Reformatted.
03/15/03	Reviewed and revised with the addition of ICD-9 codes.
10/15/05	Formatting change, WHEN SERVICES ARE COVERED UPDATE, WHEN SERVICES ARE NOT COVERED UPDATE, HCPCS update, definition update, and coverage revision.
01/01/06	Annual HCPCS coding update: deleted 90782, added new code 90772.
10/15/06	Scheduled review: ICD-9 code addition 995.2.
09/15/07	Review and revision to guideline; consisting of reformatting guideline, updated dosing, updated ICD-9 coding, updated internet links and updated references.
10/15/08	Review and revision to guideline; consisting of updating references.
01/01/09	Annual HCPCS coding update: deleted code 90772; added code 96372.
10/15/09	Review and revision to guideline; consisting of updating references.
08/15/10	Review and revision to guideline; consisting of adding coverage as an adjunct to Folutyn™ therapy and updating references.
07/15/11	Revision; formatting changes.
08/15/11	Review and revision to guideline; consisting of updating references.
08/15/12	Review and revision to guideline; consisting of updating position statement, precautions, reimbursement, program exceptions, definitions and references.
04/15/13	No Longer Reviewed.
10/01/15	Revision consisting of update to Program Exceptions section.
11/01/15	Revision: ICD-9 Codes deleted.

DECISION TREE: