

CYANOCOBALAMIN- cyanocobalamin injection
HF Acquisition Co LLC, DBA HealthFirst

CYANOCOBALAMIN INJECTION, USP 30000 mcg/30 mL (1000 mcg/mL) 30 mL VIAL

SPL UNCLASSIFIED

Rx only

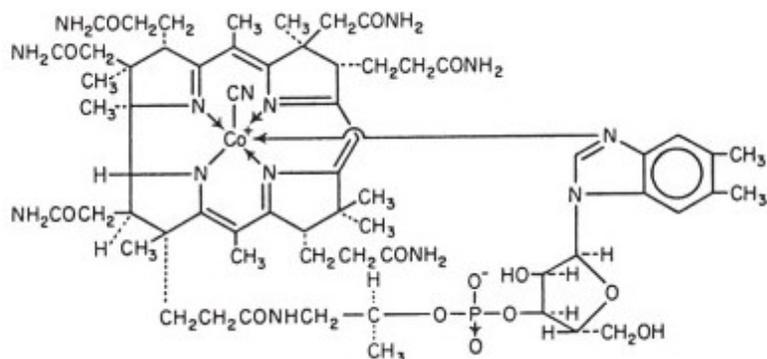
DESCRIPTION

Cyanocobalamin Injection (vitamin B12) is a sterile solution of Cyanocobalamin. Each mL contains Cyanocobalamin 1000 mcg, sodium chloride 9 mg and benzyl alcohol 0.015 mL in water for injection. Hydrochloric acid and/or sodium hydroxide may have been added to adjust the pH (range 4.5-7.0).

Cyanocobalamin appears as dark red crystals or as an amorphous or crystalline red powder. It is very hygroscopic in the anhydrous form, and sparingly soluble in water (1:80). It is stable to autoclaving for short periods at 121°C. The vitamin B12 coenzymes are very unstable in light.

The chemical name is 5,6-dimethyl-benzimidazolyl cyanocobamide; the molecular formula is C₆₃H₈₈CoN₁₄O₁₄P. The cobalt content is 4.34%. The molecular weight is 1355.39.

The structural formula is represented below.



CLINICAL PHARMACOLOGY

Vitamin B12 is essential to growth, cell reproduction, hematopoiesis, and nucleoprotein and myelin synthesis.

Cyanocobalamin is quantitatively and rapidly absorbed from intramuscular and subcutaneous sites of injection; the plasma level of the compound reaches its peak within 1 hour after intramuscular injection. Absorbed vitamin B12 is transported via specific B12 binding proteins, transcobalamin I and II to the various tissues. The liver is the main organ for vitamin B12 storage.

Within 48 hours after injection of 100 or 1000 mcg of vitamin B12, 50 to 98% of the injected dose may appear in the urine. The major portion is excreted within the first eight hours. Intravenous administration results in even more rapid excretion with little opportunity for liver storage.

Gastrointestinal absorption of vitamin B12 depends on the presence of sufficient intrinsic factor and calcium ions. Intrinsic factor deficiency causes pernicious anemia, which may be associated with subacute combined degeneration of the spinal cord.

Prompt parenteral administration of vitamin B12 prevents progression of neurologic damage.

The average diet supplies about 5 to 15 mcg/day of vitamin B12 in a protein-bound form that is available for absorption after normal digestion. Vitamin B12 is not present in foods of plant origin, but is abundant in foods of animal origin. In people with normal absorption, deficiencies have been reported only in strict vegetarians who consume no products of animal origin (including no milk products or eggs).

Vitamin B12 is bound to intrinsic factor during transit through the stomach; separation occurs in the terminal ileum in the presence of calcium, and vitamin B12 enters the mucosal cell for absorption. It is then transported by the transcobalamin binding proteins. A small amount (approximately 1% of the total amount ingested) is absorbed by simple diffusion, but this mechanism is adequate only with very large doses. Oral absorption is considered too undependable to rely on in patients with pernicious anemia or other conditions resulting in malabsorption of vitamin B12.

Cyanocobalamin is the most widely used form of vitamin B12, and has hematopoietic activity apparently identical to that of the antianemia factor in purified liver extract. Hydroxycobalamin is equally as effective as cyanocobalamin, and they share the cobalamin molecular structure.

INDICATIONS & USAGE

Cyanocobalamin is indicated for vitamin B12 deficiencies due to malabsorption which may be associated with the following conditions:

Addisonian (pernicious) anemia

Gastrointestinal pathology, dysfunction, or surgery, including gluten enteropathy or sprue, small bowel bacteria overgrowth, total or partial gastrectomy

Fish tapeworm infestation

Malignancy of pancreas or bowel

Folic acid deficiency

It may be possible to treat the underlying disease by surgical correction of anatomic lesions leading to small bowel bacterial overgrowth, expulsion of fish tapeworm, discontinuation of drugs leading to vitamin malabsorption (see PRECAUTIONS-Drug Interactions), use of a gluten-free diet in nontropical sprue, or administration of antibiotics in tropical sprue. Such measures remove the need for long-term administration of cyanocobalamin.

Requirements of vitamin B12 in excess of normal (due to pregnancy, thyrotoxicosis, hemolytic anemia, hemorrhage, malignancy, hepatic and renal disease) can usually be met with oral supplementation.

Cyanocobalamin Injection, USP is also suitable for the vitamin B12 absorption test (DOSAGE & ADMINISTRATION-Schilling test).

CONTRAINDICATIONS

Sensitivity to cobalt and/or vitamin B12 is a contraindication.

WARNINGS

Patients with early Leber's disease (hereditary optic nerve atrophy) who were treated with cyanocobalamin suffered severe and swift optic atrophy.

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

Anaphylactic shock and death have been reported after parenteral vitamin B12 administration. An intradermal test dose is recommended before Cyanocobalamin Injection, USP is administered to patients suspected of being sensitive to this drug.

This product contains Benzyl Alcohol. Benzyl Alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants.

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 patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

General

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 greater than 0.1 mg per day may result in hematologic remission in patients with vitamin B12 deficiency. Neurologic manifestations will not be prevented with folic acid, and if not treated with vitamin B12, irreversible damage will result.

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

Information for Patients

Patients with pernicious anemia should be informed that they will require monthly injections of vitamin B12 for the remainder of their lives. Failure to do so will result in return of the anemia and in development of incapacitating and irreversible damage to the nerves of the spinal cord. Also, patients should be warned about the danger of taking folic acid in place of vitamin B12, because the former may prevent anemia but allow progression of subacute combined degeneration.

A vegetarian diet which contains no animal products (including milk products or eggs) does not supply any vitamin B12. Patients following such a diet, should be advised to

take oral vitamin B12 regularly. The need for vitamin B12 is increased by pregnancy and lactation. Deficiency has been recognized in infants of vegetarian mothers who were breast fed, even though the mothers had no symptoms of deficiency at the time.

Laboratory Tests

During the initial treatment of patients with pernicious anemia, serum potassium must be observed closely the first 48 hours and potassium replaced if necessary.

Hematocrit, reticulocyte count, vitamin B12, folate and iron levels should be obtained prior to treatment. Hematocrit and reticulocyte counts should be repeated daily from the fifth to seventh days of therapy and then frequently until the hematocrit is normal. If folate levels are low, folic acid should also be administered. If reticulocytes have not increased after treatment or if reticulocyte counts do not continue at least twice normal as long as the hematocrit is less than 35%, diagnosis or treatment should be reevaluated. Repeat determinations of iron and folic acid may reveal a complicating illness that might inhibit the response of the marrow.

Patients with pernicious anemia have about 3 times the incidence of carcinoma of the stomach as the general population, so appropriate tests for this condition should be carried out when indicated.

Drug/Laboratory Test Interactions

Persons taking most antibiotics, methotrexate and pyrimethamine invalidate folic acid and vitamin B12 diagnostic blood assays.

Colchicine para-aminosalicylic acid and heavy alcohol intake for longer than 2 weeks may produce malabsorption of vitamin B12.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term studies in animals to evaluate carcinogenic potential have not been done. There is no evidence from long-term use in patients 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.

Pregnancy

Teratogenic Effects: Pregnancy Category C

Adequate and well-controlled studies have not been done in pregnant women. However, vitamin B12 is an essential vitamin and requirements are increased during pregnancy. Amounts of vitamin B12 that are recommended by the Food and Nutrition Board, National Academy of Science-National Research Council for pregnant women (4 mcg daily) should be consumed during pregnancy.

Nursing Mothers

Vitamin B12 is known to be excreted in human milk. Amounts of vitamin B12 that are recommended by the Food and Nutrition Board, National Academy of Science-National Research Council for lactating women (4 mcg daily) should be consumed during lactation.

Pediatric Use

Intake in children should be in the amount (0.5 to 3 mcg daily) recommended by the

ADVERSE REACTIONS

Generalized

Anaphylactic shock and death have been reported with administration of parenteral vitamin B12 (see WARNINGS).

Cardiovascular

Pulmonary edema and congestive heart failure early in treatment; peripheral vascular thrombosis.

Hematological

Polycythemia vera

Gastrointestinal

Mild transient diarrhea

Dermatological

Itching; transitory exanthema

Miscellaneous

Feeling of swelling of entire body

OVERDOSAGE

No overdosage has been reported with this drug.

DOSAGE & ADMINISTRATION

Avoid using the intravenous route. Use of this product intravenously will result in almost all of the vitamin being lost in the urine.

Pernicious Anemia

Parenteral vitamin B12 is the recommended treatment and will be required for the remainder of the patient's life. The oral form is not dependable. A dose of 100 mcg daily for 6 or 7 days should be administered by intramuscular or deep subcutaneous injection. If there is clinical improvement and if a reticulocyte response is observed, the same amount may be given on alternate days for seven doses, then every 3 to 4 days for another 2 to 3 weeks. By this time hematologic values should have become normal. This regimen should be followed by 100 mcg monthly for life. Folic acid should be administered concomitantly if needed.

Patients with Normal Intestinal Absorption

Where the oral route is not deemed adequate, initial treatment similar to that for patients with pernicious anemia may be indicated depending on the severity of the deficiency. Chronic treatment should be with an oral B12 preparation. If other vitamin deficiencies are present, they should be treated.

Schilling Test

The flushing dose is 1000 mcg.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

CYANOCOBALAMIN INJECTION is supplied in the following dosage forms

NDC 51662-1394-1 CYANOCOBALAMIN INJECTION, USP 30000 mcg/30 mL (1000 mcg/mL) 30 mL VIAL

NDC 51662-1394-2 Pouch containing a single CYANOCOBALAMIN INJECTION, USP 30000 mcg/30 mL (1000 mcg/mL) 30 mL VIAL

NDC 51662-1394-3 Case of 10 pouches - CYANOCOBALAMIN INJECTION, USP 30000 mcg/30 mL (1000 mcg/mL) 30 mL VIAL

HF Acquisition Co LLC, DBA HealthFirst
Mukilteo, WA 98275

Also supplied in the following manufacture supplied dosage forms

Cyanocobalamin Injection, USP 1000 mcg/mL is available in the following packages:

NDC 0143-9621-25 1 mL Vial Boxes of 25 Vials

NDC 0143-9620-10 10 mL Multiple Dose Vial Boxes of 10 Vials

NDC 0143-9619-10 30 mL Multiple Dose Vial Boxes of 10 Vials

Storage

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

PROTECT FROM LIGHT.

To report SUSPECTED ADVERSE REACTIONS, contact West-Ward Pharmaceuticals Corp. at 1-877-845-0689, or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For Product Inquiry call 1-877-845-0689.

Manufactured by:

HIKMA FARMACÊUTICA (PORTUGAL), S.A.

Estrada do Rio da Mó, 8, 8A e 8B - Fervença - 2705-906 Terrugem SNT, PORTUGAL

Distributed by:

WEST-WARD

A HIKMA COMPANY

Eatontown, NJ 07724 USA

Revised June 2017

PIN350-WES/3

PRINCIPAL DISPLAY PANEL - VIAL LABEL

NDC 0143-9619-01 30 mL Multiple Dose Vial

Cyanocobalamin
Injection, USP Rx only

30,000 mcg/30 mL
(1,000 mcg/mL)

For INTRAMUSCULAR or
SUBCUTANEOUS USE ONLY
Contains Benzyl Alcohol
as a Preservative

Each mL contains: Cyanocobalamin
1,000 mcg, Sodium Chloride 9 mg,
Benzyl Alcohol 0.015 mL in Water for
Injection. pH 4.5-7.0 adjusted with
Hydrochloric Acid and/or Sodium
Hydroxide, if needed. Contains no
more than 200 mcg/L of aluminum.
WARNING: PROTECT FROM LIGHT.
Store at 20° to 25°C (68° to 77°F).
USUAL DOSAGE: See package insert.

Distr. by:  WEST-WARD



(01)0301439619017
PLB751-WES/1

Lot:
Exp:

Non-varnish area

PRINCIPAL DISPLAY PANEL - SERIALIZED LABELING



(01) 00351662139417

(17) 201130

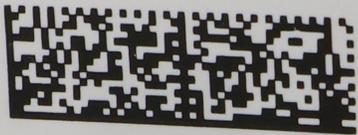
(21) 67164539829

(10) 1805248.1

See manufacturer's package insert

Distributed by HF Acquisition Co., LLC

Mukilteo, WA 98275



RX ONLY

NDC 0143-9619-01 30 mL Multiple Dose Vial

Cyanocobalamin
Injection, USP Rx only

30,000 mcg/30 mL

(1,000 mcg/mL)

For INTRAMUSCULAR or
SUBCUTANEOUS USE ONLY
Contains Benzyl Alcohol
as a Preservative

Each mL contains: Cyanocobalamin
1,000 mcg; Sodium Chloride 9 mg

Principal Display Panel - 51662-1394-2 - Pouch Labeling

CYANOCOBALAMIN INJECTION, USP 30,000 mcg/30 mL (1,000 mcg/mL) 30 mL VIAL

NDC : 51662-1394-2
LOT : 12345
EXP : 2025-01-01

(01) 00351662139424
(10) 12345
(17) 250101
(21) 153665411973

FOR INTRAMUSCULAR OR SUBCUTANEOUS USE ONLY. CONTAINS BENZYL ALCOHOL AS A PRESERVATIVE. WARNING: PROTECT FROM LIGHT. STORE AT 20° TO 25°C (68° TO 77°F), EXCURSIONS PERMITTED TO 15° TO 30°C (59° TO 86°F) [SEE USP CONTROLLED ROOM TEMPERATURE]. USUAL DOSAGE: SEE PACKAGE INSERT.

See manufacturer's package insert

ORIGINAL MFG NDC : 0143-9619-10
RX ONLY

Manufactured by HF Acquisition Co., LLC
Mukilteo, WA 98275



Principal Display Panel - 51662-1394-3 - Case Labeling

(01)00351662139431
(17)230919
(21)351662141212
(10)HF1234TESTING

SEE MANUFACTURE'S INSERT
DISTRIBUTED BY HF ACQUISITIONS CO., LLC
MUKILTEO, WA 98275

RX ONLY



CYANOCOBALAMIN INJECTION, USP 30,000 mcg/30 mL (1,000 mcg/mL) 30 mL VIAL (BOX OF 10)

NDC: 51662-1394-3
 LOT: 12345
 EXP: 2025-01-01

(01) 00351662139431
 (10) 12345
 (17) 250101
 (21) 29610756386

CASE

FOR INTRAMUSCULAR OR SUBCUTANEOUS USE ONLY. CONTAINS BENZYL ALCOHOL AS A PRESERVATIVE. WARNING: PROTECT FROM LIGHT. STORE AT 20° TO 25°C (68° TO 77°F), EXCURSIONS PERMITTED TO 15° TO 30°C (59° TO 86°F) [SEE USP CONTROLLED ROOM TEMPERATURE]. USUAL DOSAGE: SEE PACKAGE INSERT.

See manufacturer's package insert

ORIGINAL MFG NDC: 0143-9619-10

RX ONLY

Manufactured by HF Acquisition Co., LLC
 Mukilteo, WA 98275



CYANOCOBALAMIN

cyanocobalamin injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:51662-1394(NDC:0143-9619)
Route of Administration	INTRAMUSCULAR, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CYANOCOBALAMIN (UNII: P6YC3EG204) (CYANOCOBALAMIN - UNII:P6YC3EG204)	CYANOCOBALAMIN	1000 ug in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BENZYL ALCOHOL (UNII: LKG8494WBH)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51662-1394-1	30 mL in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product	10/18/2019	
2	NDC:51662-1394-3	10 in 1 CASE	01/12/2021	
2	NDC:51662-1394-2	1 mL in 1 POUCH; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA080515	10/18/2019	

Labeler - HF Acquisition Co LLC, DBA HealthFirst (045657305)

Registrant - HF Acquisition Co LLC, DBA HealthFirst (045657305)

Establishment

Name	Address	ID/FEI	Business Operations
HF Acquisition Co LLC, DBA HealthFirst		045657305	relabel(51662-1394)

Revised: 1/2024

HF Acquisition Co LLC, DBA HealthFirst