

Not to be sold by retail without the prescription of a Registered Medical Practitioner

Prescribing Information

1. Generic Name

Methylcobalamin Injection

(Brand Name: MEGO® Injection)

2. Qualitative and Quantitative Composition

Each ml contains:

Methylcobalamin IP 500 mcg.

Benzyl Alcohol IP (as preservative) 2% w/v.

Water for Injection IP q.s.

Overages are added to compensate loss on storage.

3. Dosage Form and Strength

Dosage Form: Injection.

Dosage Strength: Methylcobalamin 500 mcg per 1 ml ampoule.

4. Clinical Particulars

4.1 Therapeutic Indication

MEGO Injection is indicated for the treatment of peripheral neuropathies including diabetic neuropathy in adult patients.

MEGO Injection is also indicated in the management of megaloblastic anemia caused by vitamin B12 deficiency in adults.

4.2 Posology and Method of Administration

Peripheral Neuropathies: The usual dosage for adults is 1 ampule (500 mcg of methylcobalamin) daily, administered by intramuscular (I.M.) or intravenous (I.V.) infusion route 3 times a week. The dosage may be adjusted depending on the patient's age and symptoms. Injectable therapy is usually given for 4 to 8 consecutive weeks; followed by, therapy can be continued with oral preparations.

Megaloblastic Anemia: The usual dosage for adults is 1 ampule (500 mcg of methylcobalamin) daily, administered by I.M. or I.V. infusion route 3 times a week. After about 2 months of therapy, the dose should be reduced to a single administration of 1 ampule at 1 to 3 months intervals for maintenance therapy.

Or, as prescribed by the Physician.

Direction / Handling Conditions

I.M. Administration: Following cautions should be exercised to avoid adverse effects on tissues or nerves. Avoid repeated injection at the same site. Do not inject in densely innervated site. If insertion of the injection needle causes intense pain or if blood flows back into the syringe, withdraw the needle immediately and inject at a different site.

I.V. Infusion Administration: MEGO Injection should not be given as a direct, undiluted I.V. injection as it may give rise to dizziness, fainting, and possible tissue irritation. MEGO Injection must be diluted prior to I.V. administration with a suitable/compatible diluent such as dextrose, saline or similar I.V. infusion solutions. The solution should be used within 4 hours after dilution. I.V. infusion may be administered over a period of at least 30 minutes.

Pharmaceutical Precautions

Each ampoule is for single use only. Methylcobalamin is susceptible to photolysis. It should be used promptly after the package is opened, and caution should be taken so as not to expose the ampoules to direct light. The unused portion, if any, should be discarded.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if solution is not clear or has suspended matter. The diluted solution for infusion should not be used if crystals or precipitates are observed.

4.3 Contraindications

MEGO Injection is contraindicated in the following:

- Patients with known or suspected hypersensitivity to methylcobalamin or to any component of the formulation.
- Neonates or premature infants.
- Existing hypervitaminosis.

4.4 Special Warnings and Precautions for Use

Test Dose: Before therapy with MEGO Injection is instituted, a test dose is recommended to ascertain possibility of hypersensitivity to ingredients of MEGO Injection. Serious acute hypersensitivity reactions may require the use of subcutaneous epinephrine and other emergency measures.

Allergic Reactions: Use caution in the management of patients with known anaphylactic reactions to hydroxocobalamin or cyanocobalamin or methylcobalamin. Consideration should be given to use of alternative therapies, if available. Allergic reactions may include anaphylaxis, chest tightness, edema, angioneurotic edema, urticaria, pruritus, dyspnea, and rash.

Immune Response: Antibodies to hydroxocobalamin-transcobalamin II complex have developed during hydroxocobalamin therapy. Arrhythmias secondary to hypokalaemia have occurred at the beginning of parenteral treatment with hydroxocobalamin. This may happen with methylcobalamin therapy also.

Photolysis: Methylcobalamin is susceptible to photolysis. It should be used promptly after the package is opened, and caution should be taken so as not to expose the ampoules to direct light.

Renal and Hepatic Impairment: This product has not been studied in hepatic and renal impairment patients. It is recommended to monitor renal and hepatic functions while patient is on this therapy.

4.5 Drug Interactions

Oral Contraceptives: Serum concentrations of methylcobalamin may be decreased by use of oral contraceptives.

Chloramphenicol: Chloramphenicol should not be used with methylcobalamin. Parenteral chloramphenicol may attenuate the effect of vitamin B12 in anemia.

Other Drugs: Metformin, H2 receptor antagonists (cimetidine, ranitidine, etc.), aminoglycosides, colchicine, aminosalicic acid, anticonvulsants and alcohol decrease absorption of vitamin B12.

Drug/Laboratory Test Interactions: Persons taking most antibiotics, methotrexate and pyrimethamine invalidate vitamin B12 diagnostic blood assays.

4.6 Use in Special Populations

Pregnant Women

Pregnancy Category C. Adequate and well-controlled studies have not been done in pregnant women. Thus, MEGO Injection can be administered during pregnancy only at the recommendation of the physician.

Lactating Women

Vitamin B12 is known to be excreted in human milk. Caution should be exercised when this product is administered to a nursing woman. Nursing mothers should not use this preparation unless clearly needed and recommended by physician.

Pediatric Patients

This product has not been studied in children and thus, not indicated for use in pediatric population.

Geriatric Patients

Generally, dose adjustment is not required in the geriatric population with normal body functions (provided there is no severe renal and/or hepatic impairment).

4.7 Effect on Ability to Drive and Use Machines

With methylcobalamin, no studies have been performed on effect on the ability to drive and use machines; usually, no specific precautions are necessary. However, patients should be advised not to drive or operate machinery if affected by dizziness.

4.8 Undesirable Effects

Anaphylactoid Reaction: Anaphylactoid reaction such as decrease in blood pressure or dyspnea may occur. Patients should be carefully observed. In the event of such symptoms, treatment should be discontinued immediately and appropriate measures taken.

Other Adverse Reactions: Hypersensitivity, rash, erythema, pruritus, dizziness, agitation, anxiety, headache, hot sensation, diaphoresis, and pain/induration at the site of I.M. injection. Pulmonary edema, congestive heart failure (CHF), peripheral vascular thrombosis, polycythemia vera (bone marrow disorder), mild transient diarrhea, itching, transitory exanthema, feeling of swelling of entire body have also been reported with parenteral vitamin B-containing substances.

4.9 Overdose

No overdose has been reported with methylcobalamin injection. In the event of overdose, treatment should be symptomatic and supportive. Hemodialysis may be effective in such circumstances.

5. Pharmacological Properties

5.1 Mechanism of Action

Methylcobalamin regulates nerve function and reduces plasma homocysteine levels by following mechanisms:

1. Methylcobalamin promotes myelination (phospholipid synthesis): Methylcobalamin promotes the synthesis of lecithin, the main constituent of medullary sheath lipid and increases myelination of neurons in rat tissue culture more than cobamamide does.

2. Methylcobalamin promotes axonal transport and axonal regeneration: Methylcobalamin normalizes axonal skeletal protein transport in sciatic nerve cells from rat models with streptozotocin-induced diabetes mellitus. It exhibits neuropathologically and electrophysiologically inhibitory effects on nerve degeneration in neuropathies induced by drugs, such as adriamycin, acrylamide, and vincristine (in rats and rabbits), models of axonal degeneration in mice and neuropathies in rats with spontaneous diabetes mellitus.

3. Methylcobalamin is a kind of endogenous coenzyme B12: Methylcobalamin plays an important role in transmethylation as a coenzyme of methionine synthetase in the synthesis of methionine from homocysteine. Thus, it reduces plasma homocysteine levels.

4. Methylcobalamin is well transported to nerve cell organelles, and promotes nucleic acid and protein synthesis: Methylcobalamin is better transported to nerve cell organelles than cyanocobalamin in rats. Also, Methylcobalamin promotes nucleic acid and protein synthesis in rats more than cobamamide does.

Methylcobalamin increases erythrocytes production by following mechanisms:

Methylcobalamin promotes the maturation and division of erythroblasts, thereby alleviating anemia. It is well known that vitamin B12 deficiency may cause specific megaloblastic anemia. Methylcobalamin promotes nucleic acid synthesis in bone marrow and promotes the maturation and division of erythroblasts, thereby increasing erythrocyte production. Methylcobalamin brings about a rapid recovery of diminished red blood cell, hemoglobin, and hematocrit in vitamin B12-deficient rats.

5.2 Pharmacodynamic Properties

Methylcobalamin is the neurologically active form of vitamin B12. In many cases, liver does not convert cyanocobalamin, the commonly available form of vitamin B12, into adequate amounts of methylcobalamin. Nutritional inadequacies, enzyme defects, and pathological changes in tissues can all contribute to a reduced ability of the body to accomplish the synthesis of the active forms of vitamin B12 from cyanocobalamin. MEGO Injection provides the readymade (active) form of vitamin B12 i.e., methylcobalamin. Methylcobalamin is useful to regulate various neurological defects such as neuropathies including diabetic neuropathy. Methylcobalamin is also effective in the treatment of megaloblastic anemia caused by vitamin B12 deficiency.

5.3 Pharmacokinetic Properties

Absorption: Methylcobalamin was administered by I.M. or I.V. route to 12 healthy adult male volunteers at a single dose of 500 mcg. The time to reach peak plasma concentration (T_{max}) was 0.9 hour after I.M. administration and 3 minute after I.V. administration, and the increment in peak serum total vitamin B12 concentration (C_{max}) was 22.4 ng/ml after I.M. administration and 85 ng/ml after I.V. administration.

Distribution: Vitamin B12 is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. Vitamin B12 is stored in the liver. Vitamin B12 diffuses across the placenta and also appears in breast milk.

Metabolism and Excretion: Elimination is primarily through the bile; however, excess methylcobalamin is excreted unchanged in the urine. Vitamin B12 undergoes extensive enterohepatic recycling and is excreted in the bile. Part of a dose is excreted in the urine, most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. Elimination half-life is 27.1 hours (single-dose I.V. administration) and 29.0 hours (single-dose I.M. administration).

6. Nonclinical Properties

6.1 Animal Toxicology

Repeated dose toxicity: A total of 48 Sprague-Dawley rats were randomly assigned to receive, intravenously, 1, 5, 25 or 100 mg/kg of cyanocobalamin (6 males and 6 females in each group) three times per week until completion of the study at 182 days (26 weeks). The animals were weekly examined and blood samples were taken at days 1, 85 and 182 for cyanocobalamin determination. Finally, all animals survived throughout the study period and had similar growth rates. No evidence of toxicity was detected by a detailed weekly examination of animals during the study period. Therefore the no-observed-adverse-effect-level (NOAEL) can be established at least at 100 mg/kg under the test conditions.

Carcinogenicity: Vitamin B12 (as cyanocobalamin or hydroxocobalamin) has a long history of safe use even at high doses. A tumour promoting effect of vitamin B12 has been reported in one

study in rats. Rats kept on a methionine deficient diet supplemented with 5 µg/100 g vitamin B12 and treated with the carcinogen p-dimethylaminobenzene (DAB) had a higher incidence of hepatomas compared to the group without supplemental vitamin B12. A control group receiving the supplemented diet without DAB showed no hepatic tumours. In another study, the effect of methylcobalamin and cyanocobalamin on the growth of Walker's carcinosarcoma and on the longevity of rats with implanted Zajdela ascites hepatoma cells has been studied. Study reported reduced survival of rats upon treatment with both compounds.

7. Description

MEGO Injection is dark red coloured, clear solution filled in 1ml amber snap off break glass ampoule with white ring.

Each 1 ml ampoule of MEGO Injection contains 500 mcg of methylcobalamin for I.M. or I.V. infusion use.

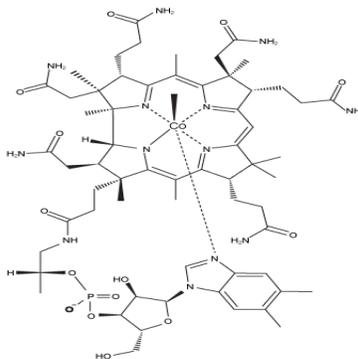
Methylcobalamin appears as dark red crystals or crystalline powder. It is sparingly soluble in water, slightly soluble in ethanol and practically insoluble in acetonitrile.

Molecular Weight: 1344.38 g/mol.

Molecular Formula: C₆₃H₉₁CoN₁₃O₁₄P.

Chemical Name: Methyl-5, 6-dimethylbenzimidazolylcobalamin.

Structural Formula:



Inactive ingredients (excipients) of MEGO Injection contain Sodium Acetate, Benzyl Alcohol, and Glacial Acetic Acid.

8. Pharmaceutical Particulars

8.1 Incompatibilities

MEGO Injection should not be mixed with any other solution/injection for which physical and chemical compatibility has not been established.

8.2 Shelf-life

18 months.

8.3 Packaging Information

1 ml glass ampoule.

8.4 Storage and Handling Instructions

Protect from light. Store at a temperature not exceeding 25°C.

Keep out of reach of children.

9. Patient Counseling Information

Administration Instructions to Patients

- Instruct patient not to remove medication from its original packaging. Also, not to expose the ampoules to direct light because methylcobalamin is susceptible to photolysis; this leads to degradation of the methylcobalamin.
- Instruct patients not to change their medication dose or schedule without consulting doctor or pharmacist. Do not exceed the recommended dose or duration of treatment.
- Instruct patient not to take I.M. injection at the same site every time. The injection site must be changed for each dose.
- Instruct patients not to share their medication with others even though it has been prescribed for same disease/condition. Also, not to use medication prescribed for others.
- Instruct patients not to use solution if it is not clear or has suspended matter.

10. Details of Manufacturer

M/s. Nitin Lifesciences Ltd.,
Rampur Road, Paonta Sahib,
Dist. Sirmour – 173025, Himachal Pradesh, India.

11. Details of Permission or License Number with Date

Manufacturing license No. MB/05/209 dated 07/03/2012.

12. Date of Revision

February 2021.

Marketed by:



Division of

BLUE CROSS LABORATORIES PVT LTD.

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