

Nervon™

(MECOBALAMIN)

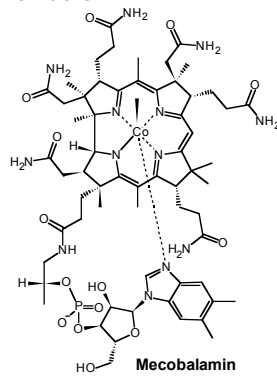
Tablets 500mcg

Injection 500mcg I.M./I.V.

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DESCRIPTION

NERVON (Mecobalamin) is a B₁₂ containing coenzyme with an active methyl base. It plays an important role in red blood cell formation, methylation reaction, brain and nervous system functions and immune system functions. Chemically, mecobalamin is described as α (5,6-Dimethylbenzimidazolyl)-Co-methyl-cobamide. The molecular formula is C₆₃H₉₁CoN₁₃O₁₄P and the structural formula is :



QUALITATIVE & QUANTITATIVE COMPOSITION

NERVON (Mecobalamin) is available for administration as:

NERVON Tablets 500mcg
Each film-coated tablet contains:
Mecobalamin JP...500mcg

NERVON I.M./I.V. Injection 500mcg
Each 1mL ampoule contains:
Mecobalamin JP...500mcg

CLINICAL PHARMACOLOGY

Mechanism of Action

1. Mecobalamin is the one and only homologue of Vitamin B₁₂ found in the brain that participates in transmethylation. Mecobalamin is well transported to nerve cell organelles than cyanocobalamin and plays the role of coenzyme in the synthesis of methionine from homocysteine. It is also involved in the synthesis of thymidine from deoxyuridine thus promoting nucleic acid protein synthesis.
2. Mecobalamin normalizes axonal transport of skeletal protein in sciatic nerve cells. It exhibits neuropathologically and electrophysiologically inhibitory effects on nerve degeneration in neuropathies induced by drugs such as adriamycin, acrylamide and vincristine.
3. Mecobalamin promotes the synthesis of lecithin, the main constituent of medullary sheath lipid, by increasing methionine synthetase activity, thus promoting myelination (phospholipid synthesis).
4. Mecobalamin restores end-plate potential early induction by increasing nerve fiber excitability in the crushed sciatic nerve. In addition, mecobalamin normalizes diminished brain tissue levels of acetylcholine.

5. Mecobalamin promotes nucleic acid synthesis in the bone marrow and promotes the maturation and division of erythroblasts thereby improving anemia, thus increasing erythrocyte production.

Pharmacokinetics

Vitamin B₁₂ substances bind to intrinsic factor, a glycoprotein secreted by the gastric mucosa and are then actively absorbed from the gastrointestinal tract. Vitamin B₁₂ is extensively bound (80%) to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. After oral administration of single doses of 1200mcg or 1500mcg of mecobalamin dose dependent peak plasma concentrations were reached in 3 hours in both cases. After a single I.M or I.V dose of 500mcg, the time required for the serum total vitamin B₁₂ level to reach a peak (T_{max}) was 0.9 ± 0.1 hours after I.M and immediately to 3 min after I.V administration. The area under the blood concentration-time curve (AUC) at 144 hours after administration was 204.1 ± 12.9hr.ng/mL after I.M administration and 358.6 ± 34.4hr.ng/mL after I.V administration. The increment in peak serum total vitamin B₁₂ level (C_{max}) was 22.4 ± 1.1ng/mL after I.M administration and 85.0 ± 8.9ng/mL after I.V administration. Vitamin B₁₂ is stored in the liver (50%), excreted in the bile and undergoes extensive enterohepatic recycling. Some of the B₁₂ secreted in the bile is excreted in the feces while the other part is excreted in the urine (40-80%), most of it in the first 8 hours. Vitamin B₁₂ diffuses across the placenta and also appears in breast milk.

THERAPEUTIC INDICATIONS

NERVON (Mecobalamin) is indicated for the treatment of:

1. Peripheral neuropathies.
2. Megaloblastic anemia caused by vitamin B₁₂ deficiency.

DOSAGE AND ADMINISTRATION

NERVON (Mecobalamin) tablets can be taken with or without food. The dosage may be adjusted depending on patient's age and symptoms.

Peripheral neuropathies

Tablets: The usual adult dosage for oral use is 3 tablets (1500mcg) daily in three divided doses.

Injection: The usual dosage for adults is 1 ampoule (500mcg of mecobalamin) a day administered intramuscularly or intravenously three times a week.

Megaloblastic anemia

The usual dosage for adults is 1 ampoule (500mcg of mecobalamin) a day administered intramuscularly or intravenously three times a week. After approximately 2 months of medication, the dose should be reduced to a single administration of NERVON (Mecobalamin) ampoule at 1 to 3 months intervals for maintenance therapy.

Instructions for use: The cut point of the ampoule should be wiped with alcohol swab before opening. In intramuscular administration, care should be exercised to avoid adverse

effects on tissues or nerves. Repeated injections at the same site should be avoided. Do not inject at innervated site. In case of severe pain after insertion of injection or if blood flows back into the syringe, withdraw the needle immediately and inject at a different site.

ADVERSE REACTIONS

Generally mecobalamin is well tolerated. However a few side effects like GI discomfort (including anorexia, nausea or diarrhea) and rash may be seen.

CONTRAINDICATIONS

Mecobalamin is contraindicated in patients who are hypersensitive to this drug or any component of this product or other B₁₂ containing products.

PRECAUTIONS

Mecobalamin injection should not be used over a period of months if there is lack of satisfactory clinical response in patients with megaloblastic anemia probably due to vitamin B₁₂ deficiency or with peripheral neuropathies.

Pregnancy and Lactation

Mecobalamin is not recommended in pregnant and lactating women.

Drug Interactions

- Decreased GI tract absorption with neomycin, aminosalicylic acid, H₂-blockers and colchicine.
- Reduced serum concentrations with oral contraceptives.
- Reduced effects in anemia with parenteral chloramphenicol.
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OVERDOSAGE

Mecobalamin has excellent tolerability. Treatment is unlikely to be needed in cases of over dose.

STORAGE AND INSTRUCTIONS

Store at 25°C (Excursions permitted between 15°C-30°C). Protect from light and moisture.

NERVON (Mecobalamin) Injection is stored in light protective packs (LPP). Light protective packs ensures quality during storage. This pack should be opened only prior to use. If ampoules are kept out of the LPP the drug will decompose upon exposure to light.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

NERVON (Mecobalamin) 500mcg Tablets is available in blister pack of 30's.

NERVON (Mecobalamin) 500mcg I.M./I.V. Injection is available in blister pack of 10x1mL ampoules.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

**Please read the contents carefully before use.
This package insert is continually updated from time to time.**

Manufactured by:

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