Cobalmin 0.5mg Film-coated Tablet

Composition: Each film coated tablet contains mecobalamin 0.5 mg

Product Description: A round, white film-coated tablet.

Pharmacodynamics

(1) Mecobalamin is a kind of endogenous coenzyme B12:

As a coenzyme of methionine synthetase, mecobalamin plays an important role in transmethylation in the synthesis of methionine from homocysteine.

(2) Mecobalamin is well transported to nerve cell organelles, and promotes nucleic acid and protein synthesis:

Experiments in rats show that mecobalamin is better transported to nerve cell organelles than cyanocobalamin and promotes nucleic acid and protein synthesis more than cobamamide does. Experiments with cells from the brain origin and spinal nerve cells in rats also show mecobalamin to be involved in the synthesis of thymidine from deoxyuridine, promotion of deposited folic acid utilization and metabolism of nucleic acid.

(3) Mecobalamin promotes axonal transport and axonal regeneration:

In rat models with streptozotocin-induced diabetes mellitus, mecobalamin normalizes axonal skeletal protein transport in sciatic nerve cells. Mecobalamin 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.

(4) Mecobalamin promotes myelination (phospholipid synthesis) :

Mecobalamin promotes the synthesis of lecithin which is the main constituent of medullary sheath lipid. It also increases myelination of neurons in rat tissue culture more than cobamamide does.

(5) Mecobalamin restores delayed synaptic transmission and diminished neurotransmitters back to normal:

Mecobalamin restores end-plate potential induction early by increasing nerve fiber excitability in the crushed sciatic nerve in rats. In addition, mecobalamin normalizes diminished levels of acetylcholine in brain tissue of rats fed with a choline-deficient diet.

Pharmacokinetics

(1) Absorption

Vitamin B12 substances bind to intrinsic factor, a glycoprotein secreted by the gastric mucosa, and are then actively absorbed from the gastrointestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy. Absorption from the gastrointestinal tract can also occur by passive diffusion; little of the vitamin present in food is absorbed in this manner although the process becomes increasingly important with larger amounts such as those used therapeutically.

(i) Single-dose administration

When mecobalamin was administered orally to healthy adult male volunteers at single doses of 120 μg and 1,500 μg) during fasting, the peak serum total vitamin B12 concentration was reached after 3 hrs for both doses, and this was dose-dependent. Note) A single dose of 1,500 μg is unapproved.

(ii) Repeated-dose administration

When mecobalamin was administered orally to healthy adult male volunteers at a dose of 1,500μg daily for 12 consecutive weeks, the serum concentration increased for the first 4 weeks after administration, rising to about twice as high as the initial value. Thereafter, there was a gradual increase which peaked at about 2.8 times the initial value at the 12th week of dosing. The serum concentration declined after the last administration (12 weeks), but was still about 1.8 times the initial value 4 weeks after the last administration.

(2) 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.

(3) Excretion

Vitamin B12 is excreted in the bile, and undergoes extensive enterohepatic recycling; 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.
40-80% of the cumulative amount of total B12 excreted in the urine by 24 hrs after single-dose administration was excreted within the first 8 hrs.
(4) Elimination Half-life
12.5 hrs (single-dose oral administration; calculated from the average of 24-48 hour values)

Indication
Peripheral neuropathies. Megaloblastic anemia due to vitamin B12 deficiency.

Recommended Dosage
Adult Dosage: The usual adult dosage for oral use is 3 tablets (1,500 µg of mecobalamin) daily divided into three doses. The dosage may be adjusted depending on the patient's age and symptoms.

Mode of administration
Oral

Contraindications
Hypersensitivity to mecobalamin or other components of the formulation.

Warnings and Precautions

This product should not be used aimlessly for more than one month unless it is effective.

Vitamin B12 should, if possible, not be given to patients with suspected vitamin B12 deficiency without first confirming the diagnosis. Where it is desirable to start therapy immediately, combined treatment for both deficiencies may be started once suitable samples have been taken to permit diagnosis of the deficiency, and the patient converted to the appropriate treatment once the cause of the anaemia is known. Regular monitoring of the blood is advisable.
Although the haematological symptoms of B12 deficiency and folate deficiency are similar, it is important to distinguish between them since the use of folate alone in B12-deficient megaloblastic anaemia can improve haematological symptoms without preventing aggravation of accompanying neurological symptoms, and may lead to severe nervous system sequelae such as subacute combined degeneration of the spinal cord. Use of doses greater than 10 micrograms daily may produce a haematological response in patients with folate deficiency and indiscriminate use may mask the precise diagnosis. Conversely, folate may mask vitamin B12 deficiency.

Precautions concerning use
(1) Administration: Mecobalamin is susceptible to photolysis. Light decreases the content of mecobalamin and tablets may change colour (eg. turn reddish) with exposure to moisture. Therefore, this product should be used promptly after the package is opened, and caution should be taken so as not to expose the tablets/capsules to light/moisture.
(2) Caution in handing over drug: For drugs that are dispensed in a press-through package (PTP), instruct the patient to remove the drug from the package prior to use. [It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, causing perforation and resulting in serious complications such as mediastinitis.]
Other Precautions
The prolonged use of larger doses of mecobalamin is not recommended for patients whose occupation requires the handling of mercury or mercury compounds.

Interactions with Other Medicaments
Absorption of vitamin B12 from the gastrointestinal tract may be reduced by neomycin, aminosalicylic acid, histamine H2-antagonists, omeprazole, and colchicine.
Serum concentrations may be decreased by use of oral contraceptives.
Many of these interactions are unlikely to be of clinical significance but should be taken into account when performing assays for blood concentrations.

Statement on Usage During Pregnancy and Lactation

Pregnancy

There are no data available for mecobalamin to be used in pregnant women.

Lactation

There are no data available for mecobalamin to be used in lactating women. However, since vitamin B12 is distributed into breast milk, The American Academy of Pediatrics considers its use to be usually compatible with breast feeding.

Adverse Effects / Undesirable Effects

Dermatologic Effects: Rash; In the event of such symptoms, treatment should be discontinued.
Gastrointestinal Effects: Anorexia, nausea/vomiting and diarrhea
Neurologic Effects (Central nervous system): Headache
Others:

- Anaphylactoid reaction 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.
- Hot sensation
- Diaphoresis
- Pain/induration at the site of intramuscular injection

Overdose and Treatment

There have been no reports, in the literature, of overdosage with mecobalamin.

Storage Conditions

Store below 30°C. Protect from light and moisture.

Shelf-life: 3 years from the date of manufacture.

Dosage Forms and Packaging Available

9 x 10's & 50 x10's Blister strip per box.

Product registration holder:

Advance Pharma Sdn Bhd (539885-W)
No. 28, Jalan BP 6/6, Bandar Bukit Puchong,
47120 Puchong Selangor.

Manufacturer:

AV Manufacturing SDN BHD (667760-v)
Lot 10621 (PT16700), Jalan Permata 2, Arab Malaysian Industrial Park
71800 Nilai, Negeri Sembilan.

Date of Revision of Package Insert

Nov 2019

Keep Out Of Reach Of Children